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(54) **Simultaneous detection, identification and differentiation of Eubacterial taxa using a hybridization assay**

(57) The present invention relates to a method for detection and identification of at least one micro-organism, or for the simultaneous detection of several micro-organisms in a sample, comprising the steps of:

- (i) if need be releasing, isolating or concentrating the polynucleic acids present in the sample;
- (ii) if need be amplifying the 16S-23S rRNA spacer region, or a part of it, with at least one suitable primer pair;
- (iii) hybridizing the polynucleic acids of step (i) or (ii) with at least one and preferably more than one of the spacer probes as mentioned in table 1a or equivalents of thereof, under the appropriate hy-

bridization and wash conditions, and/or with a taxon-specific probe derived from any of the spacer sequences as represented in figs. 1-103 under the same hybridization and wash conditions;

- (iv) detecting the hybrids formed in step (iii) with each of the probes used under appropriate hybridization and wash conditions;
- (v) identification of the micro-organism(s) present in the sample from the differential hybridization signals obtained in step (iv).

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Description

[0001] The present invention relates to nucleic acid probes derived from the spacer region between the 16S and 23S ribosomal ribonucleic acid (rRNA) genes, to be used for the specific detection of eubacterial organisms in a biological sample by a hybridization procedure, as well as to nucleic acid primers to be used for the amplification of said spacer region of eubacterial organisms in a biological sample. The present invention also relates to new spacer region sequences from which said probes or primers may be derived.

[0002] Since the advent of the polymerase chain reaction and some other nucleic acid amplification techniques the impact of DNA-probe technology in the diagnosis of micro-organisms in biological samples of all sorts is increasing. Being often more specific and potentially more sensitive - if an adequate amplification and/or detection system is used - the DNA probe approach may eventually replace the conventional identification techniques.

[0003] The reliability of nucleic acid based tests essentially depends on the sensitivity and specificity of the probes and/or primers used. Thus the corner stone of this type of assay is the identification of nucleic acid sequences which are unique to the group of organisms of interest.

[0004] Most of the nucleic acid based tests either described in literature and/or commercially available aim at the detection of just one particular organism in a biological sample. Since most biological samples usually may contain a great variety of clinically relevant micro-organisms, a multitude of separate assays have to be performed to detect all relevant organisms possibly present. This approach would be very expensive, laborious and time-consuming. Consequently, the number of tests actually performed in most routine diagnostic labs on a particular sample is restricted to the detection of just a few of the most relevant organisms. Therefore it would be extremely convenient to have access to a system which enables the fast, easy and simultaneous detection of a multitude of different organisms. The more organisms that can be screened for in the same assay, the more cost-effective the procedure would be.

[0005] As put forward in earlier published documents, the spacer region situated between the 16S rRNA and the 23S rRNA gene, also referred to as the internal transcribed spacer (ITS), is an advantageous target region for probe development for detection of pathogens of bacterial origin (International application WO 91/16454; Rossau et al., 1992; EP-A-0 395 292).

[0006] One of its most appreciated advantages is that sequences unique to a great variety of bacterial taxa can be found in a very limited area of the bacterial genome. This characteristic allows for an advantageous design of "probe-panels" enabling the simultaneous detection of a set of organisms possibly present in a particular type of a biological sample. Moreover, being flanked by quasi-universally conserved nucleotide sequences - more particularly located in the 3'-part of the 16S rRNA gene and the 5'-part of the 23S rRNA gene respectively - almost all spacers can be simultaneously amplified with a limited set of amplification primers. Alternatively, specific primer sets can be derived from the spacer sequences themselves, thereby allowing species- or group-specific amplifications.

[0007] The 16S-23S rRNA spacer region is a relatively short (about 200 to 1000 base pairs) stretch of DNA present in one or multiple copies in the genome of almost all eubacterial organisms. If multiple copies are present in the genome of one bacterium these copies can either be identical (as is most probably the case in some Neisseria species) or may differ from each other (as is the case for E. coli). This difference can be limited to a few nucleotides but also deletions and insertions of considerable length may be present.

[0008] Until now, spacer probes are only described and made publicly available for a limited number of organisms many of which were disclosed in international application WO 91/16454. As described above, it would be very advantageous to be able to detect simultaneously a panel of pathogens: e.g. a panel of pathogens possibly present in the same type of biological sample, or a panel of pathogens possibly causing the same type of disease symptoms, which are difficult to differentiate clinically and/or biochemically, or a panel of organisms belonging to the same taxon. In order to make the different panels as complete as possible, additional probes or sets of probes located in the spacer region and enabling the identification of at least the following bacterial groups or species are required:

- Mycobacterium species
- Listeria species
- Chlamydia species
- Acinetobacter species
- Mycoplasma species
- Streptococcus species
- Staphylococcus species
- Salmonella species
- Brucella species
- Yersinia species
- Pseudomonas species

[0009] These additional spacer probes need to be meticulously designed such that they can be used simultaneously with at least one other probe, under the same hybridization and wash conditions, allowing the detection of a particular panel of organisms.

[0010] It is thus the aim of the present invention to select probes or sets of probes, which have as target the 16S-23S rRNA spacer region, and which allow the detection and identification of at least one, and preferably more than one, of the above mentioned micro-organisms. The probes or probe sets are selected in such a way that they can be used in combination with at least one other probe, preferably also originating from the 16S-23S rRNA spacer region, under the same hybridisation and wash conditions, to allow possibly the simultaneous detection of several micro-organisms in a sample.

[0011] It is also an aim of the present invention to provide for a selection method for use in the selection of said spacer probes or probe sets.

[0012] It is also an aim of the present invention to provide a rapid and reliable hybridization method for detection and identification of at least one micro-organism in a sample, or for the simultaneous detection and identification of several micro-organisms in a sample.

[0013] It is more particularly an aim of the present invention to provide a hybridization method allowing simultaneous detection and identification of a set of micro-organisms, liable to be present in a particular type of sample.

[0014] It is more particularly an aim of the present invention to provide probes or sets of probes for the possible simultaneous detection of micro-organisms in a sample originating from respiratory tract.

[0015] It is another particular aim of the present invention to provide probes or sets of probes for the possible simultaneous detection of micro-organisms in a sample originating from cerebrospinal fluid.

[0016] It is still another particular aim of the present invention to provide probes or sets of probes for the possible simultaneous detection of micro-organisms in a sample originating from urogenital tract.

[0017] It is still another particular aim of the present invention to provide probes or sets of probes for the possible simultaneous detection of micro-organisms in a sample taken from the gastro-intestinal tract of a patient.

[0018] It is still another particular aim of the present invention to provide probes or sets of probes for the possible simultaneous detection of micro-organisms in a sample originating from food or environmental samples.

[0019] It is moreover an aim of the present invention to provide a method for detection and identification of a particular taxon in a sample, or a set of particular taxa, said taxon being either a complete genus, or a subgroup within a genus, a species or even subtypes within a species (subspecies, serovars, sequevars, biovars...).

[0020] It is more particularly an aim of the present invention to provide probes or sets of probes for the detection of Mycobacterium species and subspecies, more particularly for the detection of M. tuberculosis complex strains, Mycobacterium strains from the MAIS-complex, M. avium and M. paratuberculosis, M. intracellulare and M. intracellulare-like strains, M. scrofulaceum, M. kansasii, M. chelonae, M. gordonae, M. ulcerans, M. genavense, M. xenopi, M. simiae, M. fortuitum, M. malmoense, M. celatum and M. haemophilum.

[0021] It is also an aim of the present invention to provide probes or sets of probes for the detection of Mycoplasma strains, more particularly of M. pneumoniae and M. genitalium.

[0022] It is also an aim of the present invention to provide probes or sets of probes for the detection of Pseudomonas strains, more particularly P. aeruginosa.

[0023] It is also an aim of the present invention to provide probes or sets of probes for detection of Staphylococcus species, more particularly S. aureus and S. epidermidis.

[0024] It is also an aim of the present invention to provide probes or sets of probes for the detection of Acinetobacter strains, more particularly A. baumanii.

[0025] It is also an aim of the present invention to provide probes or sets of probes for the detection of Listeria strains, more particularly Listeria monocytogenes.

[0026] It is also an aim of the present invention to provide probes or sets of probes for the detection of Brucella strains.

[0027] It is also an aim of the present invention to provide probes or sets of probes for the detection of Salmonella strains.

[0028] It is also an aim of the present invention to provide probes or sets of probes for the detection of Chlamydia strains, more particularly C. trachomatis and C. psittaci.

[0029] It is also an aim of the present invention to provide probes or sets of probes for the detection of Streptococcus strains.

[0030] It is also an aim of the present invention to provide probes or sets of probes for the detection of Yersinia enterolitica strains.

[0031] It is also an aim of the present invention to provide primers allowing specific amplification of the 16S-23S rRNA spacer region for certain organisms. More particularly, it is an aim of the present invention to provide primers for the specific amplification of the spacer region of Mycobacterium, Chlamydia, Listeria, Brucella and Yersinia enterolitica strains.

[0032] It is also an aim of the present invention to provide new sequences of 16S-23S rRNA spacer regions from

which useful spacer probes or primers can be derived.

[0033] It is also an aim of the present invention to provide for kits for detection of at least one organism in a sample in which said probes and/or primers are used.

[0034] It is noted that for a few of the above-mentioned organisms spacer sequences have already been published in literature or in publicly accessible data-banks.

[0035] However, it should be made clear that the spacer region sequences disclosed in the current invention (figs. 1-103) are new and, in case they originate from the same species as those of which a spacer sequence was already described in the prior art, they differ to some extent from the already described sequences.

[0036] Moreover, it is the principal aim of the present invention to select, from the compilation of sequence data on spacer regions, specific probes and sets of probes enabling the detection and identification of a particular panel of organisms, be it the organisms belonging to a common taxon, or the organisms possibly present in the same type of sample.

[0037] The selection procedure usually consists of a theoretical and an experimental part. First of all, the different spacer sequences need to be aligned to those of the 'closest neighbours' or to the spacer sequences of other micro-organisms liable to be present in the same sample. This requires of course the sequence determination of the spacer region, as described in the examples. From the alignment, regions of divergence can be defined, from which probes with desired hybridization characteristics are designed, according to guidelines known to the man skilled in the art and specified in more detail below.

[0038] Secondly, the designed probes need to be tested experimentally and evaluated for their usefulness under specific hybridization conditions and/or in combination with other probes. Experimental testing can be done according to any hybridization method known in the art, but a preferred assay for the simultaneous testing of different probes under the same conditions is the reverse hybridization assay. A specific format for reverse hybridization of different probes simultaneously used in the current invention is the LiPA (Line Probe Assay) as described below.

[0039] Upon experimental testing unexpected hybridization behaviour may show up when the probes are hybridized to the target nucleic acid, and specific probe adaptations may be required.

[0040] Moreover, specificity and sensitivity of the probes need to be tested with a large collection of strains, both belonging to the taxon to be detected and belonging to other taxa. Due to genome heterogeneity in the spacer region, or the existence of multiple spacer regions with different sequences in the same organism, it is quite often necessary to sequence spacer regions of additional strains; or to sequence additional spacer regions in the same strain, and redesign the probes according to the new sequence data in order to obtain a better sensitivity and/or specificity (see e.g. example 3). In some cases it may be necessary or preferable to use several probes for the same organism (see e.g. example 2 and 7). Also, upon sequencing the spacer region, some organisms may show unexpected (un)relatedness, which may lead to a revision of strain classification contrary to classical taxonomic criteria (see e.g. examples 2 and 7).

[0041] In conclusion, the experimental part of the probe selection procedure is indispensable and complementary to the theoretical part. Probe design, especially under the fixed conditions of reverse hybridization (the same conditions for each probe) is not straightforward and probes have to be evaluated meticulously before they can be used in a reverse hybridization format. Therefor, probes cannot always be simply derived on a theoretical basis from a known gene sequence.

[0042] For designing probes with desired characteristics the following useful guidelines may be followed.

[0043] Because the extent and specificity of hybridization reactions such as those described herein are affected by a number of factors, manipulation of one or more of those factors will determine the exact sensitivity and specificity of a particular probe, whether perfectly complementary to its target or not. The importance and effect of various assay conditions, explained further herein, are known to those skilled in the art.

[0044] First, the stability of the [probe : target] nucleic acid hybrid should be chosen to be compatible with the assay conditions. This may be accomplished by avoiding long A and T rich sequences, by terminating the hybrids with G:C base pairs, and by designing the probe with an appropriate Tm. The beginning and end points of the probe should be chosen so that the length and %GC result in a Tm about 2-10°C higher than the temperature at which the final assay will be performed. The base composition of the probe is significant because G-C base pairs exhibit greater thermal stability as compared to A-T base pairs due to additional hydrogen bonding. Thus, hybridization involving complementary nucleic acids of higher G-C content will be stable at higher temperatures.

[0045] Conditions such as ionic strength and incubation temperature under which a probe will be used should also be taken into account in constructing a probe. It is known that hybridization will increase as the ionic strength of the reaction mixture increases, and that the thermal stability of the hybrids will increase with increasing ionic strength. On the other hand, chemical reagents, such as formamide, urea, DMSO and alcohols, which disrupt hydrogen bonds, will increase the stringency of hybridization. Destabilization of the hydrogen bonds by such reagents can greatly reduce the Tm. In general, optimal hybridization for synthetic oligonucleotide probes of about 10-50 bases in length occurs approximately 5°C below the melting temperature for a given duplex. Incubation at temperatures below the optimum

may allow mismatched base sequences to hybridize and can therefore result in reduced specificity.

[0046] It is desirable to have probes which hybridize only under conditions of high stringency. Under high stringency conditions only highly complementary nucleic acid hybrids will form; hybrids without a sufficient degree of complementarity will not form. Accordingly, the stringency of the assay conditions determines the amount of complementarity needed between two nucleic acid strands forming a hybrid. Stringency is chosen to maximize the difference in stability between the hybrid formed with the target and the nontarget nucleic acid. In some examples of the current invention, e.g. when highly related organisms need to be differentiated, it may be necessary to detect single base pair changes. In those cases, conditions of very high stringency are needed.

[0047] Second, probes should be positioned so as to minimize the stability of the [probe : nontarget] nucleic acid hybrid. This may be accomplished by minimizing the length of perfect complementarity to non-target organisms, avoiding GC rich regions of homology to non-target sequences, and by positioning the probe to span as many destabilizing mismatches as possible. Whether a probe sequence is useful to detect only a specific type of organism depends largely on the thermal stability difference between [probe:target] hybrids and [probe:nontarget] hybrids. In designing probes, the differences in these Tm values should be as large as possible (e.g. at least 2°C and preferably 5°C).

[0048] The length of the target nucleic acid sequence and, accordingly, the length of the probe sequence can also be important. In some cases, there may be several sequences from a particular region, varying in location and length, which will yield probes with the desired hybridization characteristics. In other cases, one sequence may be significantly better than another which differs merely by a single base. While it is possible for nucleic acids that are not perfectly complementary to hybridize, the longest stretch of perfectly complementary base sequence will normally primarily determine hybrid stability. While oligonucleotide probes of different lengths and base composition may be used, oligonucleotide probes preferred in this invention are between about 10 to 50 bases in length and are sufficiently homologous to the target nucleic acid.

[0049] Third, regions in the target DNA or RNA which are known to form strong internal structures inhibitory to hybridization are less preferred. Likewise, probes with extensive selfcomplementarity should be avoided. As explained above, hybridization is the association of two single strands of complementary nucleic acids to form a hydrogen bonded double strand. It is implicit that if one of the two strands is wholly or partially involved in a hybrid that it will be less able to participate in formation of a new hybrid. There can be intramolecular and intermolecular hybrids formed within the molecules of one type of probe if there is sufficient self complementarity. Such structures can be avoided through careful probe design. By designing a probe so that a substantial portion of the sequence of interest is single stranded, the rate and extent of hybridization may be greatly increased. Computer programs are available to search for this type of interaction. However, in certain instances, it may not be possible to avoid this type of interaction.

[0050] The probes of the present invention are designed for attaining optimal performance under the same hybridization conditions so that they can be used in sets for simultaneous hybridization; this highly increases the usability of these probes and results in a significant gain in time and labour. Evidently, when other hybridization conditions should be preferred, all probes should be adapted accordingly by adding or deleting a number of nucleotides at their extremities. It should be understood that these concomitant adaptations should give rise to essentially the same result, namely that the respective probes still hybridize specifically with the defined target. Such adaptations might also be necessary if the amplified material should be RNA in nature and not DNA as in the case for the NASBA system.

[0051] The hybridization conditions can be monitored relying upon several parameters, such as the nature and concentration of the components of the media, and the temperatures under which the hybrids are formed and washed.

[0052] The hybridization and wash temperature is limited in upper value depending on the sequence of the probe (its nucleic acid composition, kind and length). The maximum hybridization or wash temperature of the probes described in the present invention ranges from 40°C to 60°C, more preferably from 45°C to 55°C, in the specific hybridization and wash media as described in the Examples section. At higher temperatures duplexing (= formation of the hybrids) competes with the dissociation (or denaturation) of the hybrid formed between the probe and the target.

[0053] In a preferred hybridization medium of the invention, containing 3 x SSC and 20% formamide, hybridization temperatures can range from 45°C to 55°C, with a preferred hybridization temperature of 50°C. A preferred wash medium contains 3 x SSC and 20% formamide, and preferred wash temperatures are the same as the preferred hybridization temperatures, i.e. preferably between 45°C and 55°C, and most preferably 50°C.

[0054] However, when modifications are introduced, be it either in the probes or in the media, the temperatures at which the probes can be used to obtain the required specificity should be changed according to known relationships, such as those described in the following reference: Hames B and Higgins S (eds.). Nucleic acid hybridization. A practical approach, IRL Press, Oxford, U.K., 1985.

[0055] The selected nucleic acid probes derived from the 16S-23S rRNA spacer region and described by the present invention are listed in Table 1a (SEQ ID NO 1 to 64, 175 to 191, 193 to 201, and 210 to 212). As described in the examples section, some of these probes show a better sensitivity and/or specificity than others, and the better probes are therefore preferentially used in methods to detect the organism of interest in a biological sample. However, it is possible that for certain applications (e.g. epidemiology, substrain typing, ...) a set of probes including the less specific

and/or less sensitive probes may be very informative (see e.g. example 7).

[0056] The following definitions serve to illustrate the terms and expressions used in the different embodiments of the present invention as set out below.

[0057] The term "spacer" is an abbreviated term referring to the 16S-23S rRNA internal transcribed spacer region.

5 [0058] The term "probe" refers to single stranded sequence-specific oligonucleotides which have a sequence which is sufficiently complementary to hybridize to the target sequence to be detected.

[0059] The more specific term "spacer probe" refers to a probe as defined above having a sequence which is sufficiently complementary to hybridize to a target sequence which is located in the spacer region(s) of the organism (or group of organisms) to be detected.

10 [0060] Preferably said probes are 70%, 80%, 90%, or more than 95% homologous to the exact complement of the target sequence to be detected. These target sequences are either genomic DNA or precursor RNA, or amplified versions thereof.

15 [0061] Preferably, these probes are about 5 to 50 nucleotides long, more preferably from about 10 to 25 nucleotides. The nucleotides as used in the present invention may be ribonucleotides, deoxyribonucleotides and modified nucleotides such as inosine or nucleotides containing modified groups which do not essentially alter their hybridization characteristics. Moreover, it is obvious to the man skilled in the art that any of the below-specified probes can be used as such, or in their complementary form, or in their RNA form (wherein T is replaced by U).

20 [0062] The probes according to the invention can be formed by cloning of recombinant plasmids containing inserts including the corresponding nucleotide sequences, if need be by cleaving the latter out from the cloned plasmids upon using the adequate nucleases and recovering them, e.g. by fractionation according to molecular weight. The probes according to the present invention can also be synthesized chemically, for instance by the conventional phosphotriester method.

25 [0063] The term "complementary" nucleic acids as used herein means that the nucleic acid sequences can form a perfect base-paired double helix with each other.

[0064] The term "homologous" as used in the current application is synonymous for identical: this means that poly-nucleic acids which are said to be e.g. 80% homologous show 80% identical base pairs in the same position upon alignment of the sequences.

30 [0065] The term "polynucleic acid" corresponds to either double-stranded or single-stranded cDNA or genomic DNA or RNA, containing at least 10, 20, 30, 40 or 50 contiguous nucleotides. A polynucleic acid which is smaller than 100 nucleotides in length is often also referred to as an oligonucleotide. Single stranded polynucleic acid sequences are always represented in the current invention from the 5' end to the 3' end.

35 [0066] The term 'closest neighbour' means the taxon which is known or expected to be most closely related in terms of DNA homology and which has to be differentiated from the organism of interest.

[0067] The expression 'desired hybridization characteristics' means that the probe only hybridizes to the DNA or RNA from organisms for which it was designed, and not to DNA or RNA from other organisms (closest neighbours or organisms liable to be present in the same sample). In practice, this means that the intensity of the hybridization signal is at least two, three, four, five, ten or more times stronger with the target DNA or RNA from the organisms for which the probes were designed, as compared to non-target sequences.

40 [0068] These desired hybridization characteristics correspond to what is called later in the text "specific hybridization".

[0069] The expression "taxon-specific hybridization" or "taxon-specific probe" means that the probe only hybridizes to the DNA or RNA from the taxon for which it was designed and not to DNA or RNA from other taxa.

[0070] The term taxon can refer to a complete genus or a sub-group within a genus, a species or even subtype within a species (subspecies, serovars, sequevars, biovars...).

45 [0071] The term "specific amplification" or "specific primers" refers to the fact that said primers only amplify the spacer region from these organisms for which they were designed, and not from other organisms.

[0072] The term "sensitivity" refers to the number of false negatives: i.e. if 1 of the 100 strains to be detected is missed out, the test shows a sensitivity of $(100-1)/100\% = 99\%$.

[0073] The term "specificity" refers to the number of false positives: i.e. if on 100 strains detected, 2 seem to belong to organisms for which the test is not designed, the specificity of the test is $(100-2)/100\% = 98\%$.

50 [0074] The probes selected as being "preferential" show a sensitivity and specificity of more than 80%, preferably more than 90% and most preferably more than 95%.

[0075] The term "primer" refers to a single stranded DNA oligonucleotide sequence capable of acting as a point of initiation for synthesis of a primer extension product which is complementary to the nucleic acid strand to be copied.

55 The length and the sequence of the primer must be such that they allow to prime the synthesis of the extension products. Preferably the primer is about 5-50 nucleotides long. Specific length and sequence will depend on the complexity of the required DNA or RNA targets, as well as on the conditions of primer use such as temperature and ionic strength. The fact that amplification primers do not have to match exactly with the corresponding template sequence to warrant proper amplification is amply documented in the literature (Kwok et al., 1990).

[0076] The amplification method used can be either polymerase chain reaction (PCR; Saiki et al., 1988), ligase chain reaction (LCR; Landgren et al., 1988; Wu & Wallace, 1989; Barany, 1991), nucleic acid sequence-based amplification (NASBA; Guatelli et al., 1990; Compton, 1991), transcription-based amplification system (TAS; Kwok et al., 1989), strand displacement amplification (SDA; Duck, 1990; Walker et al., 1992) or amplification by means of QB replicase (Lizardi et al., 1988; Lomeli et al., 1989) or any other suitable method to amplify nucleic acid molecules known in the art.

[0077] The oligonucleotides used as primers or probes may also comprise nucleotide analogues such as phosphorothioates (Matsukura et al., 1987), alkylphosphorothioates (Miller et al., 1979) or peptide nucleic acids (Nielsen et al., 1991; Nielsen et al., 1993) or may contain intercalating agents (Asseline et al., 1984).

[0078] As most other variations or modifications introduced into the original DNA sequences of the invention these variations will necessitate adaptions with respect to the conditions under which the oligonucleotide should be used to obtain the required specificity and sensitivity. However the eventual results of hybridisation will be essentially the same as those obtained with the unmodified oligonucleotides.

[0079] The introduction of these modifications may be advantageous in order to positively influence characteristics such as hybridization kinetics, reversibility of the hybrid-formation, biological stability of the oligonucleotide molecules, etc.

[0080] The term "solid support" can refer to any substrate to which an oligonucleotide probe can be coupled, provided that it retains its hybridization characteristics and provided that the background level of hybridization remains low. Usually the solid substrate will be a microtiter plate, a membrane (e.g. nylon or nitrocellulose) or a microsphere (bead). Prior to application to the membrane or fixation it may be convenient to modify the nucleic acid probe in order to facilitate fixation or improve the hybridization efficiency. Such modifications may encompass homopolymer tailing, coupling with different reactive groups such as aliphatic groups, NH₂ groups, SH groups, carboxylic groups, or coupling with biotin, haptens or proteins.

[0081] The term "labelled" refers to the use of labelled nucleic acids. Labelling may be carried out by the use of labelled nucleotides incorporated during the polymerase step of the amplification such as illustrated by Saiki et al. (1988) or Bej et al. (1990) or by the use of labelled primers, or by any other method known to the person skilled in the art. The nature of the label may be isotopic (³²P, ³⁵S, etc.) or non-isotopic (biotin, digoxigenin, etc.).

[0082] The "sample" may be any biological material taken either directly from the infected human being (or animal), or after culturing (enrichment), or a sample taken from food or feed. Biological material may be e.g. expectorations of any kind, bronchoelavages, blood, skin tissue, biopsies, lymphocyte blood culture material, colonies, etc. Said samples may be prepared or extracted according to any of the techniques known in the art.

[0083] The "target" material in these samples may be either genomic DNA or precursor RNA of the organism to be detected (=target organism), or amplified versions thereof as set out above. More specifically, the nucleic acid sequence of the target material is localized in the spacer region of the target organism(s).

[0084] Detection and identification of the target material can be performed by using one of the many electrophoresis methods, hybridization methods or sequencing methods described in literature and currently known by men skilled in the art. However, a very convenient and advantageous technique for the simultaneous detection of nucleic acids possibly present in biological samples is the Line Probe Assay technique. The Line Probe Assay (LiPA) is a reverse hybridization format (Saiki et al., 1989) using membrane strips onto which several oligonucleotide probes (including negative or positive control oligonucleotides) can be conveniently applied as parallel lines.

[0085] The LiPA technique, as described by Stuyver et al. (1993) and in international application WO 94/12670, provides a very rapid and user-friendly hybridization test. Results can be read within 4 h. after the start of the amplification. After amplification during which usually a non-isotopic label is incorporated in the amplified product, and alkaline denaturation, the amplified product is contacted with the probes on the membrane and the hybridization is carried out for about 1 to 1.5 h. Consequently, the hybrids formed are detected by an enzymatic procedure resulting in a visual purple-brown precipitate. The LiPA format is completely compatible with commercially available scanning devices, thus rendering automatic interpretation of the results possible. All those advantages make the LiPA format liable for use in a routine setting.

[0086] The LiPA format is not only an advantageous tool for identification and detection of pathogens at the species level but also at higher or lower taxonomical levels. For instance, probe-configurations on LiPA strips can be selected in such a manner that they can detect a complete genus (e.g. Neisseria, Listeria, etc.) or can identify subgroups within a genus (e.g. subgroups in the Mycobacterium avium-intracellulare-scarfulaceum complex) or can in some cases even detect subtypes (subspecies, serovars, sequevars, biovars, etc. whatever is clinically relevant) within a species.

[0087] It should be stressed that the ability to simultaneously generate hybridization results with a number of probes is an outstanding benefit of the LiPA technology. In many cases the amount of information which can be obtained by a particular combination of probes greatly outnumbers the data obtained by using single probe assays. Therefor the selection of probes on the membrane strip is of utmost importance since an optimized set of probes will generate the maximum of information possible. This is more particularly exemplified further herein.

[0088] The fact that different probes can be combined on one strip also offers the possibility to conveniently cope

with a lack of sensitivity due to sequence heterogeneity in the target region of the group of organisms to be detected. Due to this heterogeneity, two or more probes may be required to positively identify all organisms of the particular group. These probes can be applied to membrane strips at different locations and the result is interpreted as positive if at least one of these probes is positive. Alternatively these probes can be applied as a mixture at the same location, hereby reducing the number of lines on a strip. This reduction may be convenient in order to make the strip more concise or to be able to extend the total number of probes on one strip. Another alternative approach, in view of its practical benefits, is the synthesis of oligonucleotides harbouring the sequences of two (or more) different probes (=degenerate probes) which then can be further processed and applied to the strip as one oligonucleotide molecule. This approach would considerably simplify the manufacturing procedures of the LiPA-strips. For example, probes with nucleotide sequences A and B are both required to detect all strains of taxon X. In the latter alternative a probe can be synthesized having the nucleotide sequence AB. This probe will have the combined characteristics of probes A and B.

[0089] By virtue of the above-mentioned properties the LiPA system can be considered as a preferential format for a hybridization method wherein several organisms need to be detected simultaneously in a sample. Moreover, as described in the examples section, the LiPA system is a preferred format for a selection method for the experimental evaluation and selection of theoretically designed probes.

[0090] However, it should be clear that any other hybridization assay, whereby different probes are used under the same hybridization and wash conditions can be used for the above-mentioned detection and/or selection methods. For example, it may be possible to immobilize the target nucleic acid to a solid support, and use mixtures of different probes, all differently labeled, resulting in a different detection signal for each of the probes hybridized to the target.

[0091] As an example, the procedure to be followed for the detection of one or more organisms in a sample using the LiPA format is outlined below :

- First, the nucleic acids of the organism(s) to be detected in the sample, is made available for amplification and/or hybridization.
- Secondly, the nucleic acids, if present, are amplified with one or another target amplification system, as specified below. Usually, amplification is needed to enhance the subsequent hybridization signal. However for some samples or some organisms amplification might not be necessary. This might also be the case if, for the detection of the hybrids formed, highly sensitive signal-amplification systems are used.
- Thirdly, eventually after a denaturation step, the nucleic acids present in the sample or the resulting amplified product are contacted with LiPA strips onto which one or more DNA-probes, allowing the detection of the organisms of interest, are immobilized, and hybridization is allowed to proceed.
- Finally, eventually after having performed a wash step, the hybrids are detected using a convenient and compatible detection system. From the hybridization signals or patterns observed the presence or absence of one or several organisms screened for in that particular biological sample can be deduced.

[0092] The amplification system used may be more or less universal, depending on the specific application needed.

[0093] By using universal primers located in the conserved flanking regions (16S and 23S gene) of the rRNA spacer, the spacer region of most if not all organisms of eubacterial origin will be amplified. The same result may be obtained by using a combination of different sets of primers with reduced universality (multiplex amplification, i.e. an amplification procedure in which two or more primer sets are used simultaneously in one and the same reaction mixture).

[0094] For some applications it may be appropriate to amplify not all organisms present in the sample but more specifically, beforehand defined taxa. This may be achieved using specific primers located either in less conserved parts of the flanking genes of the spacers (e.g. MYCP1-5 for amplification of the spacer region of mycobacteria) or located in the spacers themselves (e.g. LIS-P1-P7, BRU-P1-4, CHTR-P1-2 and YEC-P1-2 for specific amplification of the spacer region(s) of Listeria species, Brucella species, Chlamydia trachomatis, and Yersinia enterocolitica respectively).

[0095] The present invention thus provides a method for detection and identification of at least one micro-organism, or for the simultaneous detection of several micro-organisms in a sample, comprising the steps of:

- (i) if need be releasing, isolating and/or concentrating the polynucleic acids from the micro-organism(s) to be detected in the sample;
- (ii) if need be amplifying the 16S-23S rRNA spacer region, or a part of it, from the microorganism(s) to be detected, with at least one suitable primer pair;
- (iii) hybridizing the polynucleic acids of step (i) or (ii) with a set of probes comprising at least two probes, under the same hybridization and wash conditions, with said probes being selected from the sequences of table Ia or equivalents thereof and/or from taxon-specific probes derived from any of the spacer sequences represented in figs. 1-103, with said taxon-specific probe being selected such that it is capable of hybridizing under the same

hybridization and wash conditions as at least one of the probes of table 1a;

(iv) detecting the hybrids formed in step (iii);

(v) identification of the micro-organism(s) present in the sample from the differential hybridization signals obtained in step (iv).

[0096] The probes as mentioned in table 1a are all selected in such a way that they show the desired hybridization characteristics at a hybridization and wash temperature of 50°C in a preferred hybridization and wash medium of 3X SSC and 20% formamide.

[0097] The term "equivalents" of a probe, also called "variants" or "homologues" or "obvious derivatives", refers to probes differing in sequence from any of the probes specified in table 1 either by addition to or removal from any of their respective extremities of one or several nucleotides, or by changing one or more nucleotides within said sequences, or a combination of both, provided that said equivalents still hybridize with the same RNA or DNA target as the corresponding unmodified probe sequence. Said equivalents share at least 75% homology, preferably more than 80%, most preferably more than 85% homology with the corresponding unmodified probe sequence. It should be noted that, when using an equivalent of a probe, it may be necessary to modify the hybridization conditions to obtain the same specificity as the corresponding unmodified probe. As a consequence, since it is the aim of this invention to use a set of probes which work under the same hybridization and wash conditions, it will also be necessary to modify accordingly the sequence of the other probes, belonging to the same set as the original unmodified probe. These modifications can be done according to principles known in the art, e.g. such as those described in Hames B and Higgins S, (Eds): Nucleic acid hybridization. Practical approach. IRL Press, Oxford, UK, 1985.

[0098] The invention also provides for a method to select taxon-specific probes from the spacer region sequence(s) of said taxon, said probes being selected such that they show their desired hybridization characteristics under unified hybridization and wash conditions.

[0099] The term "unified" conditions means that these conditions are the same for the different probes enabling the detection of different taxa.

[0100] Preferentially, the present invention provides for a method as described above wherein at least 2 micro-organisms are detected simultaneously.

[0101] In a preferred embodiment, the set of probes as described in step (iii) is comprising at least two probes being selected from the sequences of table 1a, or equivalents thereof.

[0102] In another embodiment, the set of probes as described in step (iii) is comprising at least one probe being selected from the sequences of table 1a, or equivalents thereof, and at least one taxon-specific probe derived from any of the spacer sequences as represented in figs. 1 - 103.

[0103] In still another embodiment, the set of probes as described in step (iii) is comprising at least two taxon-specific probes derived from any of the spacer sequences as represented in figs. 1-103.

[0104] The present invention also provides for a method as described above, wherein the probes as specified in step (iii) are combined with at least one other probe, preferentially also from the 16S-23S rRNA spacer region, enabling the simultaneous detection of different pathogenic bacteria liable to be present in the same sample.

[0105] The organisms of clinical relevance present in biological samples may vary considerably depending on the origin of the sample. The most common pathogenic bacteria which may be found in sputum samples, or in samples originating from the respiratory tract, are :

- Moraxella catarrhalis
- Streptococcus pneumoniae
- Haemophilus influenzae
- Pseudomonas aeruginosa
- Mycoplasma pneumoniae
- Acinetobacter species
- Mycobacterium species
- Staphylococcus aureus
- Legionella pneumophila

[0106] A LiPA-strip harbouring spacer-probes enabling the detection of most if not all of these organisms would be extremely beneficial for reasons explained above.

[0107] Evidently, this also applies for other biological samples, as there are :

cerebrospinal fluid, urogenital samples, gastrointestinal samples, blood, urine, food products, soil, etc. For example, a preferred panel for cerebrospinal fluid would contain probe combinations enabling the detection and differentiation of the following organisms :

- Neisseria meningitidis
- Streptococcus pneumoniae
- Streptococcus agalactiae
- Listeria monocytogenes
- Mycobacterium tuberculosis

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[0108] For some of the above mentioned organisms, spacer probes were already designed in a previous patent application (WO 91/16454). In order to be able to detect most pathogens possibly present in a sample in a single test, the probes of the present invention may be combined with at least one of the probes of WO 91/16454, or their obvious derivatives as specified in WO 91/16454. For clarity, these probes are listed hereafter:

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Neisseria gonorrhoeae: NGI1: CGATGCGTCGTATTCTACTTCGC
15 NGI2: TTCGTTACCTACCCGTTGACTAAGTAAGCAAAAC

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Neisseria meningitidis: NMI1: GGTCAAGTGTGACGTCGCCCTG
NMI2: GTTCTTGGTCAAGTGTGACGTC
NMI3: GCGTTCGTTATAGCTATCTACTGTGC
NMI4: TGCCTCGATATTGCTATCTACTGTGCA
NMI5: TTTTGTCTTGGTCAAGTGTGACGTCGCCCTGAA
25 TGGATTCTGTTCCATT
NMI6: TTTGCCTAACATTCCGTTGACTAGAACATCAGAC

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Haemophilus ducreyi HDI1: TTATTATGCGCGAGGCATATTG
Branhamella catarrhalis BCI1: TTAAACATCTTACCAAAG
35 BCI2: TTGATGTTAAACTTGCTTGGTGGGA
Bordetella pertussis BPI1: CCACACCCATCCTCTGGACAGGCTT
Haemophilus influenzae HII1: ACGCATCAAATTGACCGCACTT
40 HII2: ACTTGAAAGTAAAAGTAAAG
Streptococcus agalactiae SAI1: AATCGAAAGGTTCAAATTGTT
SAI2: GGAAACCTGCCATTGCGTCTT
45 SAI3: TCCACGATCTAGAAATAGATTGTAGAA
SAI4: TCTAGTTAAAGAAACTAGGTT
Streptococcus pneumoniae SPI1: GTGAGAGATCACCAAGTAATGCA
50 SPI2: AGGAACTGCGCATTGGTCTT
SPI3: GAGTTATGACTGAAAGGTCAGAA

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[0109] The invention thus provides for a method as described above, wherein said sample is originating from the respiratory tract, and wherein the set of probes as defined in step (iii) comprises at least one probe chosen from the following spacer probes:

MYC-ICG-1 :	ACTGGATAGTGGTTGCGAGCATCTA	(SEQ ID NO 1)
MYC-ICG-22 :	CTTCTGAATAGTGGTTGCGAGCATCT	(SEQ ID NO 2)
5 MTB-ICG-1 :	GGGTGCATGACAACAAAGTTGGCCA	(SEQ ID NO 3)
MTB-ICG-2 :	GACTTGTCCAGGTGTTGTCCCAC	(SEQ ID NO 4)
10 MTB-ICG-3 :	CGGCTAGCGGTGGCGTGTCT	(SEQ ID NO 5)
MAI-ICG-1 :	CAACAGCAAATGATTGCCAGACACAC	(SEQ ID NO 6)
MIL-ICG-11 :	GAGGGGTTCCCGTCTGTAGTG	(SEQ ID NO 7)
15 MIL-ICG-22 :	TGAGGGGTTCTCGTCTGTAGTG	(SEQ ID NO 8)
MAC-ICG-1 :	CACTCGGTGATCCGTGTGGA	(SEQ ID NO 9)
20 MAV-ICG-1 :	TCGGTCCGTCCGTGTGGAGTC	(SEQ ID NO 10)

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	MAV-ICG-22 :	GTGGCCGGCGTTCATCGAAA	(SEQ ID NO 11)
5	MIN-ICG-1 :	GCATAGTCCTTAGGGCTGATGCGTT	(SEQ ID NO 12)
	MIN-ICG-2 :	GCTGATGCGTTCGTCGAAATGTGTA	(SEQ ID NO 13)
	MIN-ICG-22 :	CTGATGCGTTCGTCGAAATGTGT	(SEQ ID NO 14)
	MIN-ICG-222 :	TGATGCGTTCGTCGAAATGTGT	(SEQ ID NO 15)
10	MIN-ICG-2222 :	GGCTGATGCGTTCGTCGAAATGTGTA	(SEQ ID NO 16)
	MAL-ICG-1 :	ACTAGATGAACCGCGTAGTCCTGT	(SEQ ID NO 17)
	MHEF-ICG-1 :	TGGACGAAAACC GG GTGCACAA	(SEQ ID NO 18)
15	MAH-ICG-1 :	GTGTAATTCTTTTAAC TCTTG TGTAAGTAAGTG	
			(SEQ ID NO 19)
20	MCO-ICG-11 :	TGGCCGGCGTGTTCATCGAAA	(SEQ ID NO 20)
	MTH-ICG-11 :	GCACTTCAATTGGTGAAGTGCGAGCC	(SEQ ID NO 21)
	MTH-ICG-2 :	GCGTGGTCTTCATGCCGG	(SEQ ID NO 22)
	MEF-ICG-11 :	ACGCGTGGTCCTCGTGG	(SEQ ID NO 23)
25	MSC-ICG-1 :	TCGGCTCGTTCTGAGTGGTGTC	(SEQ ID NO 24)
	MKA-ICG-1 :	GATGCGTTGCTACGGGTAGCGT	(SEQ ID NO 25)
	MKA-ICG-2 :	GATGCGTTGCCTACGGGTAGCGT	(SEQ ID NO 26)
30	MKA-ICG-3 :	ATGCGTTGCCCTACGGGTAGCGT	(SEQ ID NO 27)
	MKA-ICG-4 :	CGGGCTCTGTTCGAGAGTTGTC	(SEQ ID NO 28)
	MKA-ICG-5 :	CCCTCAGGGATTCTGGGTGTTG	(SEQ ID NO 182)
35	MKA-ICG-6 :	GGACTCGTCCAAGAGTGTGTTG	(SEQ ID NO 183)
	MKA-ICG-7 :	TCGGGCTTGGCCAGAGCTGTT	(SEQ ID NO 184)
	MKA-ICG-8 :	GGGTGCGAACAGCAAGCGA	(SEQ ID NO 185)
40	MKA-ICG-9 :	GATGCGTTGCCCTACGGG	(SEQ ID NO 186)
	MKA-ICG-10 :	CCCTACGGTAGCGTGTCTTTG	(SEQ ID NO 187)
	MCH-ICG-1 :	GGTGTGGACTTGACTTCTGAATAG	(SEQ ID NO 29)
45	MCH-ICG-2 :	CGGCAAAACGTCGGACTGTCA	(SEQ ID NO 30)
	MCH-ICG-3 :	GGTGTGGTCCTTGACTTATGGATAG	(SEQ ID NO 210)
	MGO-ICG-1 :	AACACCCTCGGGTGCTGTCC	(SEQ ID NO 31)
50	MGO-ICG-2 :	GTATGCGTTGTCGTCGCGGC	(SEQ ID NO 32)
	MGO-ICG-5 :	CGTGAGGGGTACCGTCTGTAG	(SEQ ID NO 33)
	MUL-ICG-1 :	GGTTCGGGATGTTGTCCCACC	(SEQ ID NO 175)
55	MGV-ICG-1 :	CGACTGAGGTCGACGTGGTGT	(SEQ ID NO 176)

5	MGV-ICG-2 :	GGTGTGAGCATTGAATAGTGGTTGC	(SEQ ID NO 177)
	MGV-ICG-3 :	TGGGGCCGCGTGTTCGTCAAA	(SEQ ID NO 211)
10	MXE-ICG-1 :	GTTGGGCAGCAGGCAGTAACC	(SEQ ID NO 178)
	MSI-ICG-1 :	CCGGCAACGGTTACGTGTTC	(SEQ ID NO 179)
15	MFO-ICG-1 :	TCGTTGGATGCCCTCGCACCT	(SEQ ID NO 180)
	MFO-ICG-2 :	ACTTGGCGTGGGATGCGGGAA	(SEQ ID NO 181)
20	MML-ICG-1 :	CGGATCGATTGAGTGCTTGTCCC	(SEQ ID NO 188)
	MML-ICG-2 :	TCTAAATGAACGCAGTGCCTGATGG	(SEQ ID NO 189)
25	MCE-ICG-1 :	TGAGGGAGCCCGTGCCTGTA	(SEQ ID NO 190)
	MHP-ICG-1 :	CATGTTGGGCTTGATCGGGTGC	(SEQ ID NO 191)
30	PA-ICG 1 :	TGGTGTGCTGCGTGATCCGAT	(SEQ ID NO 34)
	PA-ICG 2 :	TGAATGTTCGTGGATGAACATTGATT	(SEQ ID NO 35)
	PA-ICG 3 :	CACTGGTGATCATTCAAGTCAAG	(SEQ ID NO 36)
35	PA-ICG 4 :	TGAATGTTCGT(G/A)(G/A)ATGAACATTGATTCTGGTC	(SEQ ID NO 37)
	PA-ICG 5 :	CTCTTCACTGGTGATCATTCAAGTCAAG	(SEQ ID NO 38)
40	MPN-ICG 1 :	ATCGGTGGTAAATTAAACCCAAATCCCTGT	(SEQ ID NO 49)
	MPN-ICG 2 :	CAGTTCTGAAAGAACATTCCGCTTTC	(SEQ ID NO 50)
45	MGE-ICG 1 :	CACCCATTAATTTTCGGTGTAAAACCC	(SEQ ID NO 51)
	Mycoplasma-ICG :	CAAAACTGAAAACGACAATCTTCTAGTTCC	(SEQ ID NO 52)
50	STAU-ICG 1 :	TACCAAGCAAAACCGAGTGAATAAGAGTT	(SEQ ID NO 53)
	STAU-ICG 2 :	CAGAAGATGCGGAATAACGTGAC	(SEQ ID NO 54)
	STAU-ICG 3 :	AACGAAGCCGTATGTGAGCATTGAC	(SEQ ID NO 55)
	STAU-ICG 4 :	GAACGTAACCTCATGTTAACGTTGACTTAT	(SEQ ID NO 56)
	ACI-ICG 1 :	GCTTAAGTGCACAGTGCTCTAAACTGA	(SEQ ID NO 57)
	ACI-ICG 2 :	CACGGTAATTAGTGTGATCTGACGAAG	(SEQ ID NO 58)

and more preferably from the following spacer probes:

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MYC-ICG-1 :	ACTGGATAGTGGTTGCGAGCATCTA	(SEQ ID NO 1)
MYC-ICG-22 :	CTTCTGAATAGTGGTTGCGAGCATCT	(SEQ ID NO 2)
5 MTB-ICG-1 :	GGGTGCATGACAACAAAGTTGGCCA	(SEQ ID NO 3)
MTB-ICG-2 :	GACTTGTCCAGGTGTTGTCCCAC	(SEQ ID NO 4)
10 MTB-ICG-3 :	CGGCTAGCGGTGGCGTGTCT	(SEQ ID NO 5)
MAI-ICG-1 :	CAACAGCAAATGATTGCCAGACACAC	(SEQ ID NO 6)

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	MIL-ICG-11 :	GAGGGGTTCCCGTCTGTAGTG	(SEQ ID NO 7)
	MIL-ICG-22 :	TGAGGGGTTCTCGTCTGTAGTG	(SEQ ID NO 8)
5	MAC-ICG-1 :	CACTCGGTGATCCGTGTGGA	(SEQ ID NO 9)
	MAV-ICG-1 :	TCGGTCCCGTCCGTGTGGAGTC	(SEQ ID NO 10)
	MAV-ICG-22 :	GTGCCCGCGTTCATCGAAA	(SEQ ID NO 11)
10	MIN-ICG-1 :	GCATAGTCCTTAGGGCTGATGCGTT	(SEQ ID NO 12)
	MAL-ICG-1 :	ACTAGATGAACCGTAGTCCTTGT	(SEQ ID NO 17)
	MCO-ICG-11 :	TGGCCGGCGTGTTCATCGAAA	(SEQ ID NO 20)
15	MTH-ICG-11 :	GCACTTCAATTGGTGAAGTGCGAGCC	(SEQ ID NO 21)
	MTH-ICG-2 :	GCGTGGTCTTCATGGCCGG	(SEQ ID NO 22)
	MEF-ICG-11 :	ACGCGTGGTCCTCGTGG	(SEQ ID NO 23)
20	MSC-ICG-1 :	TCGGCTCGTTCTGAGTGGTGTGTC	(SEQ ID NO 24)
	MKA-ICG-3 :	ATGCGTTGCCCTACGGGTAGCGT	(SEQ ID NO 27)
	MKA-ICG-4 :	CGGGCTCTGTTGAGAGAGTTGTC	(SEQ ID NO 28)
25	MKA-ICG-5 :	CCCTCAGGGATTTCTGGGTGTTG	(SEQ ID NO 182)
	MKA-ICG-6 :	GGACTCGTCCAAGAGTGTGTC	(SEQ ID NO 183)
	MKA-ICG-7 :	TCGGGCTTGGCCAGAGCTGTT	(SEQ ID NO 184)
30	MKA-ICG-8 :	GGGTGCGAACAGCAAGCGA	(SEQ ID NO 185)
	MKA-ICG-9 :	GATGCGTTGCCCTACGGG	(SEQ ID NO 186)
	MKA-ICG-10 :	CCCTACGGGTAGCGTGTCTTTG	(SEQ ID NO 187)
35	MCH-ICG-1 :	GGTGTGGACTTGACTCTGAATAG	(SEQ ID NO 29)
	MCH-ICG-2 :	CGGCAAAACGTCGGACTGTCA	(SEQ ID NO 30)
	MCH-ICG-3 :	GGTGTGGCCTTGACTTATGGATAG	(SEQ ID NO 210)
40	MGO-ICG-5 :	CGTGAGGGTCATCGTCTGTAG	(SEQ ID NO 33)
	MUL-ICG-1 :	GGTTTCGGGATGTTGTCCCACC	(SEQ ID NO 175)
	MGV-ICG-1 :	CGACTGAGGTCGACGTGGTGT	(SEQ ID NO 176)
45	MGV-ICG-2 :	GGTGTGAGCATTGAATAGTGGTTGC	(SEQ ID NO 177)
	MGV-ICG-3 :	TCGGGCCGCGTGTTCGTCAA	(SEQ ID NO 211)
	MXE-ICG-1 :	GTTGGCAGCAGGAGTAACC	(SEQ ID NO 178)
50	MSI-ICG-1 :	CCGGCAACGGTTACGTGTT	(SEQ ID NO 179)
	MFO-ICG-1 :	TCGTTGGATGCCCTCGCACCT	(SEQ ID NO 180)
	MFO-ICG-2 :	ACTTGGCGTGGGATGCAGGAA	(SEQ ID NO 181)
55	MML-ICG-1 :	CGGATCGATTGAGTGCTTGTCCC	(SEQ ID NO 188)

MML-ICG-2 :	TCTAAATGAACGCAC TGCCGATGG	(SEQ ID NO 189)
MCE-ICG-1 :	TGAGGGAGCCC GTGCCTGTA	(SEQ ID NO 190)
MHP-ICG-1 :	CATGTTGGGCTTGATCGGGTGC	(SEQ ID NO 191)
PA-ICG 1 :	TGGTGTGCTGCGTGATCCGAT	(SEQ ID NO 34)
PA-ICG 4 :	TGAATGTTCGT(G/A)(G/A)ATGAACATTGATTCTGGTC	(SEQ ID NO 37)
PA-ICG 5 :	CTCTTCACTGGTGATCATTCAAGTCAAG	(SEQ ID NO 38)
MPN-ICG 1 :	ATCGGTGGTAAATTAAACCCAAATCCCTGT	(SEQ ID NO 49)
MPN-ICG 2 :	CAGTTCTGAAAGAACATTCCGCTTCTTC	(SEQ ID NO 50)
MGE-ICG 1 :	CACCCATTAAATTTTCGGTGTAAAACCC	(SEQ ID NO 51)
Mycoplasma-ICG :	CAAAA CTGAAAACGACAATCTTCTAGTTCC	(SEQ ID NO 52)
STAU-ICG 1 :	TACCAAGCAAACCGAGTGAAATAAAGAGTT	(SEQ ID NO 53)
STAU-ICG 2 :	CAGAAGATGCGGAATAACGTGAC	(SEQ ID NO 54)
STAU-ICG 3 :	AACGAAGCCGTATGTGAGCATTGAC	(SEQ ID NO 55)
STAU-ICG 4 :	GAACGTAACTTCATGTTAACGTTGACTTAT	(SEQ ID NO 56)
ACI-ICG 1 :	GCTTAAGTGCACAGTGCTCTAAACTGA	(SEQ ID NO 57)
ACI-ICG 2 :	CACGGTAATTAGTGTGATCTGACGAAG	(SEQ ID NO 58)

35 or equivalents of said probes,

and/or wherein the set of probes comprises at least one taxon-specific probe derived from the spacer region sequence corresponding to one of the micro-organisms to be detected in said sample, said spacer region sequence being chosen from any of the sequences as represented by SEQ ID NO 76 to 106, 157 to 174, 124, 125, 111 to 115, 139 to 144, or 126 to 130,

40 and with said probes or equivalents being possibly used in combination with any probe detecting at least one of the following organisms: Haemophilus influenzae, Streptococcus pneumoniae, Moraxella catarrhalis or Bordetella pertussis.

[0110] The above mentioned probes of the invention are designed for the detection of Mycobacterium species (SEQ ID NO 1 to 33 and 175 to 191), of Pseudomonas aeruginosa (SEQ ID NO 34 to 38), of Mycoplasma species (SEQ ID NO 49 to 52), of Staphylococcus aureus (SEQ ID NO 53 to 56) and of Acinetobacter baumanii (SEQ ID NO 57 and 58).

[0111] Preferentially, at least two, three, four, five, six, seven, eight or more of said probes are used simultaneously.

[0112] The invention also relates to a method as described above, wherein said sample is a sample taken from the cerebrospinal fluid, and wherein the set of probes as described in step (iii) comprises at least one probe chosen from the following spacer probes:

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MYC-ICG-1 : ACTGGATAGTGGTTGCGAGCATCTA (SEQ ID NO 1)

MYC-ICG-22 : CTTCTGAATAGTGGTTGCGAGCATCT (SEQ ID NO 2)

MTB-ICG-1 : GGGTGATGACAACAAAGTTGGCCA (SEQ ID NO 3)

MTB-ICG-2 : GACTTGTCCAGGTGTTGTCCCAC (SEQ ID NO 4)

MTB-ICG-3 : CGGCTAGCGGTGGCGTGTCT (SEQ ID NO 5)

LIS-ICG 1 : CAAGTAACCGAGAATCATCTGAAAGTGAATC (SEQ ID NO 39)

LMO-ICG 1 : AAACAAACCTTACTCGTAGAAGTAAATTGGTTAAG

(SEQ ID NO 40)

LMO-ICG 2 : TGAGAGGTAGTACTCTCAGTATGTTGTT (SEQ ID NO 41)

LMO-ICG 3 AGGCACATATGCTTGAAGCATCGC (SEQ ID NO 42)

LISP-ICG-1 CGTTTCAATAAGCGATCGCACGTT (SEQ ID NO:212)

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NCV-ICG-22 CTTCTGCAATAGCTGCCAGCATCT (SEQ ID NO: 1) (SEQ ID NO: 2)

MTR-ICG-15: CCCTTCCATGAGAAGAAACTTGGCA (SEQ ID NO: 3)

MTB-ICG-34: CACTTGTTCGACCTGTTCTGCCAG (SEQ ID NO: 1)

MTB-ICG-3 : CGGCTAGCGGTGGCGTGTCT (SEQ ID NO 5)

LIS-JCG 1 : CAAGTAACCGAGAACATCATCTGAAAGTGAATC (SEQ ID NO 39)

L-MO-ICG 3 : AGGCACATATGCTTGAAGCATCGC (SEQ ID NO 42)

LISP-ICG 1: CGTTTCATAAGCGATCGCACGTT (SEQ ID NO 212)

or equivalents of said probes.

and/or wherein the set of probes comprises at least one taxon-specific probe derived from the spacer region sequence corresponding to one of the micro-organisms to be detected in said sample, said spacer region sequence being chosen from any of the sequences as represented by SEQ ID NO 116, 118-121, or 213-215,

and with said probes or equivalents being possibly used in combination with any probe detecting at least one of the following organisms: *Neisseria meningitidis*, *Haemophilus influenzae* or *Streptococcus pneumoniae*.

[0113] The above mentioned probes of the invention are designed for the detection of Mycobacterium species, and more particularly Mycobacterium tuberculosis (SEQ ID NO 1 to 5), and of Listeria species, more particularly Listeria monocytogenes (SEQ ID NO 39 to 42).

[0114] Preferentially, at least two, three, four, five, six, seven, eight or more of said probes are used simultaneously.

[0115] The invention also relates to a method as described above, wherein said sample is a sample taken from the urogenital tract, and wherein the set of probes as described in step (iii) comprises at least one probe chosen from the following spacer probes:

CHTR-ICG 1 :	GGAAGAAGCCTGAGAAGGTTCTGAC	(SEQ ID NO 45)
CHTR-ICG 2 :	GCATTATATGTAAGAGCAAGCATTCTATTCA	(SEQ ID NO 46)
5 CHTR-ICG 3 :	GAGTAGCGTGGTGAGGACGAGA	(SEQ ID NO 47)
CHTR-ICG 4 :	GAGTAGCGCGGTGAGGACGAGA	(SEQ ID NO 201)
10 CHPS-ICG 1 :	GGATAACTGTCTIAGGACGGTTGAC	(SEQ ID NO 48)
MGE-ICG 1 :	CACCCATTAATTTTCGGTGTAAAACCC	(SEQ ID NO 51)
Mycoplasma-ICG :	CAAAACTGAAAACGACAATCTTCTAGTTCC	(SEQ ID NO 52)

15 or equivalents of said probes,
and/or wherein the set of probes comprises at least one taxon-specific probe derived from the spacer region sequence
corresponding to one of the micro-organisms to be detected in said sample, said spacer region sequence being chosen
from any of the sequences as represented by SEQ ID NO 122, 123, 197, 124 or 125,

20 with said probes or equivalents being possibly used in combination with any probe detecting at least one of the following
organisms: Neisseria gonorrhoeae, Haemophilus ducreyi or Streptococcus agalactiae.

[0116] The above mentioned probes of the invention are designed for the detection of Chlamydia species (SEQ ID
NO 45 to 48 and 201) and of Mycoplasma species (SEQ ID NO 51 and 52).

[0117] Preferentially, at least two, three, four, five, six or seven of said probes are used simultaneously.

[0118] The invention also relates to a method as described above, wherein said sample is a sample taken from food,
and wherein the set of probes as defined in step (iii) comprises at least one probe chosen from the following spacer
probes:

LIS-ICG 1 :	CAAGTAACCGAGAACATCATCTGAAAGTGAATC	(SEQ ID NO 39)
30 LMO-ICG 1 :	AAACAAACCTTACTTCGTAGAAGTAAATTGGTTAAG	(SEQ ID NO 40)
LMO-ICG 2 :	TGAGAGGTTAGTACTTCTCAGTATGTTGTTC	(SEQ ID NO 41)

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LMO-ICG 3 :	AGGCACTATGCTTGAAGCATCGC	(SEQ ID NO 42)	
LIV-ICG 1 :	GTTAGCATAAAATAGGTAACTATTATGACACAAGTAAC		
5		(SEQ ID NO 43)	
LSE-ICG 1 :	AGTTAGCATAAGTAGTGTAACTATTATGACACAAG	(SEQ ID NO 44)	
10	LISP-ICG 1 :	CGTTTCATAAGCGATCGCACGTT	(SEQ ID NO 212)
STAU-ICG 1 :	TACCAAGCAAAACCGAGTGAATAAAGAGTT	(SEQ ID NO 53)	
15	STAU-ICG 2 :	CAGAAGATGCGGAATAACGTGAC	(SEQ ID NO 54)
STAU-ICG 3 :	AACGAAGCCGTATGTGAGCATTGAC	(SEQ ID NO 55)	
20	STAU-ICG 4 :	GAACGTAACCTCATGTTAACGTTGACTTAT	(SEQ ID NO 56)
BRU-ICG 1 :	CGTGCCGCCCTCGTTCTCTTT	(SEQ ID NO 59)	
25	BRU-ICG 2 :	TTCGCTTCGGGGTGGATCTGTG	(SEQ ID NO 60)
BRU-ICG 3 :	GCGTAGTAGCGTTGCGTCGG	(SEQ ID NO 193)	
BRU-ICG 4 :	CGCAAGAAGCTTGCTCAAGCC	(SEQ ID NO 194)	
SALM-ICG 1 :	CAAAACTGACTTACGAGTCACGTTGAG	(SEQ ID NO 61)	
30	SALM-ICG 2 :	GATGTATGCTTCGTTATTCCACGCC	(SEQ ID NO 62)
STY-ICG 1 :	GGTCAAACCTCCAGGGACGCC	(SEQ ID NO 63)	
SED-ICG 1 :	GCGGTAATGTGTGAAAGCGTTGCC	(SEQ ID NO 64)	
35	YEC-ICG 1 :	GGAAAAGGTACTGCACGTGACTG	(SEQ ID NO 198)
YEC-ICG 2 :	GACAGCTGAAACTTATCCCTCCG	(SEQ ID NO 199)	
YEC-ICG 3 :	GCTACCTGTTGATGTAATGAGTCAC	(SEQ ID NO 200)	

and preferably from the following spacer probes:

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LIS-ICG 1 :	CAAGTAACCGAGAATCATCTGAAAGTGAATC	(SEQ ID NO 39)
LMO-ICG 3 :	AGGCACTATGCTGAAGCATCGC	(SEQ ID NO 42)
LISP-ICG 1:	CGTTTCATAAGCGATCGCACGTT	(SEQ ID NO 212)
STAU-ICG 1 :	TACCAAGCAAAACCGAGTGAATAAAGAGTT	(SEQ ID NO 53)
10 STAU-ICG 2 :	CAGAAGATGCGGAATAACGTGAC	(SEQ ID NO 54)
STAU-ICG 3 :	AACGAAGCCGTATGTGAGCATTGAC	(SEQ ID NO 55)
STAU-ICG 4 :	GAACGTAACCTCATGTTAACGTTGACTTAT	(SEQ ID NO 56)
15 BRU-ICG 2 :	TTCGCTTCGGGGTGGATCTGTG	(SEQ ID NO 60)
BRU-ICG 3 :	GCGTAGTAGCGTTGCGTCGG	(SEQ ID NO 193)
BRU-ICG 4 :	CGCAAGAAGCTTGCTCAAGCC	(SEQ ID NO 194)
20 SALM-ICG 1 :	CAAAACTGACTTACGAGTCACGTTGAG	(SEQ ID NO 61)
YEC-ICG 1 :	GGAAAAGGTACTGCACGTGACTG	(SEQ ID NO 198)
25 YEC-ICG 2 :	GACAGCTGAAACTTATCCCTCCG	(SEQ ID NO 199)
YEC-ICG 3 :	GCTACCTGTTGATGTAATGAGTCAC	(SEQ ID NO 200)

30 or equivalents of said probes,
and/or wherein the set of probes comprises at least one taxon-specific probe derived from the spacer region sequence
corresponding to one of the micro-organisms to be detected in said sample, said spacer region sequence being chosen
from any of the sequences as represented by SEQ ID NO 116, 118-121, 213-215, 139-144, 131, 132, 154, 133-138,
195 or 196,
35 with said probes or equivalents being possibly used in combination with any probe detecting strains of Campylobacter
species.
[0119] The above mentioned probes of the invention are designed for the detection of Listeria species (SEQ ID NO
39 to 44), of Staphylococcus species (SEQ ID NO 53 to 56), of Brucella species (SEQ ID NO 59, 60, 193 and 194), of
Salmonella species (SEQ ID NO 61 to 64) and of Yersinia enterocolitica (SEQ ID NO 198 to 200).
[0120] Preferentially, at least two, three, four, five, six, seven, eight or more of said probes are used simultaneously.
[0121] The invention also relates to a method as described above, wherein said sample is a sample taken from the
gastrointestinal tract of a patient, and wherein the set of probes as defined in step (iii) comprises at least one probe
chosen from the following spacer probes:

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SALM-ICG 1 :	CAAAA CTGACTTACGAGTCACGTTGAG	(SEQ ID NO 61)
SALM-ICG 2 :	GATGTATGCTTCGTTATTCCACGCC	(SEQ ID NO 62)
STY-ICG 1 :	GGTCAAACCTCCAGGGACGCC	(SEQ ID NO 63)
SED-ICG 1 :	GCGGTAATGTGTGAAAGCGTTGCC	(SEQ ID NO 64)
YEC-ICG 1 :	GGAAAAGGTACTGCACGTGACTG	(SEQ ID NO 198)
YEC-ICG 2 :	GACAGCTGAAACTTATCCCTCCG	(SEQ ID NO 199)
YEC-ICG 3 :	GCTACCTGTTGATGTAATGAGTCAC	(SEQ ID NO 200)

and preferably from the following spacer probes:

SALM-ICG 1 :	CAAAA CTGACTTACGAGTCACGTTGAG	(SEQ ID NO 61)
YEC-ICG 1 :	GGAAAAGGTACTGCACGTGACTG	(SEQ ID NO 198)
YEC-ICG 2 :	GACAGCTGAAACTTATCCCTCCG	(SEQ ID NO 199)
YEC-ICG 3 :	GCTACCTGTTGATGTAATGAGTCAC	(SEQ ID NO 200)

or equivalents of said probes,

and/or wherein the set of probes comprises at least one taxon-specific probe derived from the spacer region sequence corresponding to one of the micro-organisms to be detected in said sample, said spacer region sequence being chosen from any of the sequences as represented by SEQ ID NO 133-138 or 195-196,

with said probes or equivalents being possibly used in combination with any probe detecting Campylobacter species.

[0122] The above mentioned probes of the invention are designed to detect Salmonella species (SEQ ID NO 61 to 64) and Yersinia enterocolitica (SEQ ID NO 198 to 200).

[0123] Preferentially, at least two, three, four, five, six or seven of said probes are used simultaneously.

[0124] The invention also relates to the use of the selected probes or their equivalents for the detection of specific bacterial taxa, said taxa being either a complete genus, or a subgroup within a genus, a species, or even a subtype within a species.

[0125] The invention thus provides for a method as described above to detect and identify one or more strains of Mycobacterium species and subspecies in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

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5	MYC-ICG-1 :	ACTGGATAGTGGTTGCGAGCATCTA	(SEQ ID NO 1)
	MYC-ICG-22 :	CTTCTGAATAGTGGTTGCGAGCATCT	(SEQ ID NO 2)
10	MTB-ICG-1 :	GGGTGCATGACAACAAAGTTGGCCA	(SEQ ID NO 3)
	MTB-ICG-2 :	GACTTGTCCAGGTGTTGTCCCAC	(SEQ ID NO 4)
15	MTB-ICG-3 :	CGGCTAGCGGTGGCGTGTCT	(SEQ ID NO 5)
	MAI-ICG-1 :	CAACAGCAAATGATTGCCAGACACAC	(SEQ ID NO 6)
20	MIL-ICG-11 :	GAGGGGTTCCCGTCTGTAGTG	(SEQ ID NO 7)
	MIL-ICG-22 :	TGAGGGGTTCTCGTCTGTAGTG	(SEQ ID NO 8)
25	MAC-ICG-1 :	CACTCGGTGATCCGTGTGGA	(SEQ ID NO 9)
	MAV-ICG-1 :	TCGGTCCGTCCGTGTGGAGTC	(SEQ ID NO 10)
30	MAV-ICG-22 :	GTGGCCGGCGTTCATCGAAA	(SEQ ID NO 11)
	MIN-ICG-1 :	GCATAGTCCTAGGGCTGATGCGTT	(SEQ ID NO 12)
35	MIN-ICG-2 :	GCTGATGCGTTCGTCGAAATGTGTA	(SEQ ID NO 13)
	MIN-ICG-22 :	CTGATGCGTTCGTCGAAATGTGT	(SEQ ID NO 14)
	MIN-ICG-222 :	TGATGCGTTCGTCGAAATGTGT	(SEQ ID NO 15)
40	MIN-ICG-2222 :	GGCTGATGCGTTCGTCGAAATGTGTAA	(SEQ ID NO 16)
	MAL-ICG-1 :	ACTAGATGAACCGCGTAGTCCTGT	(SEQ ID NO 17)
45	MHEF-ICG-1 :	TGGACGAAAACCGGGTGCACAA	(SEQ ID NO 18)
	MAH-ICG-1 :	GTGTAATTCTTTTAACCTTGTGTAAAGTAAGTG	

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			(SEQ ID NO 19)
5	MCO-ICG-11 :	TGGCCGGCGTGTTCATCGAAA	(SEQ ID NO 20)
	MTH-ICG-11 :	GCACTTCAATTGGTGAAGTGCGAGCC	(SEQ ID NO 21)
	MTH-ICG-2 :	GCGTGGTCTTCATGCCGG	(SEQ ID NO 22)
10	MEF-ICG-11 :	ACGCGTGGTCCTCGTGG	(SEQ ID NO 23)
	MSC-ICG-1 :	TCGGCTCGTTCTGAGTGGTGTC	(SEQ ID NO 24)
	MKA-ICG-1 :	GATGCGTTGCTACGGGTAGCGT	(SEQ ID NO 25)
15	MKA-ICG-2 :	GATGCGTTGCCTACGGGTAGCGT	(SEQ ID NO 26)
	MKA-ICG-3 :	ATGCGTTGCCCTACGGGTAGCGT	(SEQ ID NO 27)
	MKA-ICG-4 :	CGGGCTCTGTTGAGAGTTGTC	(SEQ ID NO 28)
	MKA-ICG-5 :	CCCTCAGGGATTTCTGGGTGTTG	(SEQ ID NO 182)
20	MKA-ICG-6 :	GGACTCGTCCAAGAGTGTGTCC	(SEQ ID NO 183)
	MKA-ICG-7 :	TCGGGCTTGGCCAGAGCTGTT	(SEQ ID NO 184)
	MKA-ICG-8 :	GGGTGCGAACAGCAAGCGA	(SEQ ID NO 185)
25	MKA-ICG-9 :	GATGCGTTGCCCTACGGG	(SEQ ID NO 186)
	MKA-ICG-10 :	CCCTACGGTAGCGTGTCTTTG	(SEQ ID NO 187)
	MCH-ICG-1 :	GGTGTGGACTTGACTTCTGAATAG	(SEQ ID NO 29)
30	MCH-ICG-2 :	CGGCAAAACGTCGGACTGTCA	(SEQ ID NO 30)
	MGO-ICG-1 :	AACACCCCTGGGTGCTGTCC	(SEQ ID NO 31)
	MGO-ICG-2 :	GTATGCGTTGTCGTTCGCGGC	(SEQ ID NO 32)
35	MGO-ICG-5 :	CGTGAGGGGTACCGTCTGTAG	(SEQ ID NO 33)
	MUL-ICG-1 :	GGTTTCGGGATGTTGTCCCACC	(SEQ ID NO 175)
	MGV-ICG-1 :	CGACTGAGGTCGACGTGGTGT	(SEQ ID NO 176)
40	MGV-ICG-2 :	GGTGTGAGCATTGAATAGTGGTTGC	(SEQ ID NO 177)
	MXE-ICG-1 :	GTTGGGCAGCAGGCAGTAACC	(SEQ ID NO 178)
	MSI-ICG-1 :	CCGGCAACGGTTACGTGTT	(SEQ ID NO 179)
45	MFO-ICG-1 :	TCGTTGGATGGCCTCGCACCT	(SEQ ID NO 180)
	MFO-ICG-2 :	ACTTGGCGTGGGATGCGGGAA	(SEQ ID NO 181)
	MML-ICG-1 :	CGGATCGATTGAGTGCTTGTCCC	(SEQ ID NO 188)
50	MML-ICG-2 :	TCTAAATGAACGCAC TGCCGATGG	(SEQ ID NO 189)
	MCE-ICG-1 :	TGAGGGAGCCCGTGCCTGTA	(SEQ ID NO 190)
	MHP-ICG-1 :	CATGTTGGGCTTGATGGGTGC	(SEQ ID NO 191)

and more preferably to at least one probe of the following restricted group of spacer probes:

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	MYC-ICG-1 :	ACTGGATAGTGGTTGCGAGCATCTA	(SEQ ID NO 1)
	MYC-ICG-22 :	CTTCTGAATAGTGGTTGCGAGCATCT	(SEQ ID NO 2)
5	MTB-ICG-1 :	GGGTGCATGACAACAAAGTTGCCA	(SEQ ID NO 3)
	MTB-ICG-2 :	GACTTGTCCAGGTGTTGTCCCAC	(SEQ ID NO 4)
	MTB-ICG-3 :	CGGCTAGCGGTGGCGTGTCT	(SEQ ID NO 5)
10	MAI-ICG-1 :	CAACAGCAAATGATTGCCAGACACAC	(SEQ ID NO 6)
	MIL-ICG-11 :	GAGGGGTTCCCGTCTGTAGTG	(SEQ ID NO 7)
	MIL-ICG-22 :	TGAGGGGTTCTCGTCTGTAGTG	(SEQ ID NO 8)
15	MAC-ICG-1 :	CACTCGGTCGATCCGTGTGGA	(SEQ ID NO 9)
	MAV-ICG-1 :	TCGGTCCGTCCGTGTGGAGTC	(SEQ ID NO 10)
	MAV-ICG-22 :	GTGGCCGGCGTTCATCGAAA	(SEQ ID NO 11)
20	MIN-ICG-1 :	GCATAGTCCTTAGGGCTGATGCGTT	(SEQ ID NO 12)
	MAL-ICG-1 :	ACTAGATGAACCGTAGTCCTTGT	(SEQ ID NO 17)
	MCO-ICG-11 :	TGGCCGGCGTGTTCATCGAAA	(SEQ ID NO 20)
25	MTH-ICG-11 :	GCACTTCAATTGGTGAAGTGCAGGCC	(SEQ ID NO 21)
	MTH-ICG-2 :	GCGTGGTCTTCATGCCGG	(SEQ ID NO 22)
	MEF-ICG-11 :	ACGCGTGGTCCTCGTGG	(SEQ ID NO 23)
30	MSC-ICG-1 :	TCGGCTCGTTCTGAGTGGTGTC	(SEQ ID NO 24)
	MKA-ICG-3 :	ATGCGTTGCCCTACGGTAGCGT	(SEQ ID NO 27)
	MKA-ICG-4 :	CGGGCTCTGTCGAGAGTTGTC	(SEQ ID NO 28)
35	MKA-ICG-5 :	CCCTCAGGGATTCTGGGTGTTG	(SEQ ID NO 182)
	MKA-ICG-6 :	GGACTCGTCCAAGAGTGTGTC	(SEQ ID NO 183)
	MKA-ICG-7 :	TCGGGCTTGGCCAGAGCTGTT	(SEQ ID NO 184)
40	MKA-ICG-8 :	GGGTGCGAACAGCAAGCGA	(SEQ ID NO 185)
	MKA-ICG-9 :	GATGCGTTGCCCTACGGG	(SEQ ID NO 186)
	MKA-ICG-10 :	CCCTACGGTAGCGTGTCTTTG	(SEQ ID NO 187)
45	MCH-ICG-1 :	GGTGTGGACTTGACTTCTGAATAG	(SEQ ID NO 29)
	MCH-ICG-2 :	CGGCAAAACGTCGGACTGTCA	(SEQ ID NO 30)
	MCH-ICG-3 :	GGTGTGGCCTTGACTTATGGATAG	(SEQ ID NO 210)
50	MGO-ICG-5 :	CGTGAGGGGTATCGTGTAG	(SEQ ID NO 33)
	MUL-ICG-1 :	GGTTTCGGGATGTTGTCCCACC	(SEQ ID NO 175)
	MGV-ICG-1 :	CGACTGAGGTCGACGTGGTGT	(SEQ ID NO 176)
55	MGV-ICG-2 :	GGTGTGAGCATTGAATAGTGGTGC	(SEQ ID NO 177)

MGV-ICG-3 :	TCGGGCCGCGTGTTCGTCAAA	(SEQ ID NO 211)
MXE-ICG-1 :	GTTGGGCAGCAGGCAGTAACC	(SEQ ID NO 178)
MSI-ICG-1 :	CCGGCAACGGTTACGTGTT	(SEQ ID NO 179)
MFO-ICG-1 :	TCGTTGGATGGCCTCGCACCT	(SEQ ID NO 180)
MFO-ICG-2 :	ACTTGGCGTGGGATGCGGGAA	(SEQ ID NO 181)
MML-ICG-1 :	CGGATCGATTGAGTGCTTGTCCC	(SEQ ID NO 188)
MML-ICG-2 :	TCTAAATGAACGCAGTGCCTGGA	(SEQ ID NO 189)
MCE-ICG-1 :	TGAGGGAGCCCGTGCCTGTA	(SEQ ID NO 190)
MHP-ICG-1 :	CATGTTGGGCTTGATCGGGTGC	(SEQ ID NO 191)

or to equivalents of said probes,
and/or to any probe derived from SEQ ID NO 76-110, or 157-174 provided said probe hybridizes specifically to a Mycobacterium species.

[0126] The sequences represented by SEQ ID NO 76-110 and 157-174 are new.

[0127] Preferentially, at least two, three, four, five, six, seven, eight or more of said probes are used simultaneously.

[0128] As described above, the preferred restricted set of probes are those probes which showed a sensitivity and specificity of more than 80%, preferably more than 90%, most preferably more than 95%, under the specific hybridization conditions as described in the examples section.

[0129] In one specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium tuberculosis complex strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

MTB-ICG-1 :	GGGTGCATGACAACAAAGTTGGCCA	(SEQ ID NO 3)
MTB-ICG-2 :	GACTTGTCCAGGTGTTGTCCCAC	(SEQ ID NO 4)
MTB-ICG-3 :	CGGCTAGCGGTGGCGTGTCT	(SEQ ID NO 5)

or to equivalents of said probes,
and/or to any probe derived from SEQ ID NO 76 provided said probe hybridizes specifically to the M. tuberculosis complex. The M. tuberculosis complex comprises M. tuberculosis, M. bovis, M. bovis BCG, M. africanum and M. microti strains.

[0130] The sequence represented in SEQ ID NO 76 is new.

[0131] Preferentially, at least two, or three of said probes are used simultaneously.

[0132] In another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium strains from the MAIS-complex, wherein step (iii) comprises hybridizing to at least one of the following probes:

MAI-ICG-1 :	CAACAGCAAATGATTGCCAGACACAC	(SEQ ID NO 6)
MIL-ICG-11 :	GAGGGGTTCCCGTCTGTAGTG	(SEQ ID NO 7)
5 MIL-ICG-22 :	TGAGGGGTTCTCGTCTGTAGTG	(SEQ ID NO 8)
MAC-ICG-1 :	CACTCGGTGATCCGTGTGGA	(SEQ ID NO 9)
10 MAV-ICG-1 :	TCGGTCCGTCCGTGTGGAGTC	(SEQ ID NO 10)
MAV-ICG-22 :	GTGGCCGGCGTTCATCGAAA	(SEQ ID NO 11)
MIN-ICG-1 :	GCATAGTCCTTAGGGCTGATGCGTT	(SEQ ID NO 12)
15 MIN-ICG-2 :	GCTGATGCGTTCGTCGAAATGTGTA	(SEQ ID NO 13)
MIN-ICG-22 :	CTGATGCGTTCGTCGAAATGTG	(SEQ ID NO 14)
MIN-ICG-222 :	TGATGCGTTCGTCGAAATGTG	(SEQ ID NO 15)
20 MIN-ICG-2222 :	GGCTGATGCGTTCGTCGAAATGTGTA	(SEQ ID NO 16)
MAL-ICG-1 :	ACTAGATGAACCGCGTAGTCCTGT	(SEQ ID NO 17)
MHEF-ICG-1 :	TGGACGAAAACCGGGTGCACAA	(SEQ ID NO 18)
25 MAH-ICG-1 :	GTGTAATTCTTTAACTCTTGTGTAAAGTAAGTG	
		(SEQ ID NO 19)
MCO-ICG-11 :	TGGCCGGCGTGTTCATCGAAA	(SEQ ID NO 20)
30 MTH-ICG-11 :	GCACTTCAATTGGTGAAGTGCAGGCC	(SEQ ID NO 21)
MTH-ICG-2 :	GCGTGGTCTTCATGGCCGG	(SEQ ID NO 22)
MEF-ICG-11 :	ACGCGTGGTCCTCGTGG	(SEQ ID NO 23)
35 MSC-ICG-1 :	TCGGCTCGTTCTGAGTGGTGTC	(SEQ ID NO 24)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 77-100 or 108-110, provided said probe hybridizes specifically to strains from the MAIS complex. The MAIS complex as defined in this invention comprises all strains of M. avium, M. intracellulare and M. scrofulaceum and all strains closely related to the above mentioned species and not clearly belonging to another defined Mycobacterium species. The latter group of strains are defined in this invention as "MIC strains" (M. intracellulare complex).

[0133] Preferentially, at least two, three, four, five, six, seven, eight or more of said probes are used simultaneously.

[0134] In still another specific embodiment, the invention provides for a method as described above, to detect and identify one or more M. avium and M. paratuberculosis strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

MAV-ICG-1 : TCGGTCCGTCCGTGTGGAGTC (SEQ ID NO 10)

50 MAV-ICG-22 : GTGGCCGGCGTTCATCGAAA (SEQ ID NO 11)

or to equivalents of said probes,

55 and/or to any probe derived from SEQ ID NO 77 and 78 provided said probe hybridizes specifically to M. avium or M. paratuberculosis.

[0135] The sequences as represented in SEQ ID NO 77 and 78 are new.

[0136] Preferentially, this embodiment uses both probes in combination.

[0137] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium intracellulare strains and MIC-strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

5	MAI-ICG-1 :	CAACAGCAAATGATTGCCAGACACAC	(SEQ ID NO 6)
10	MIL-ICG-11 :	GAGGGGTTCCCGTCTGTAGTG	(SEQ ID NO 7)
15	MIL-ICG-22 :	TGAGGGGTTCTCGTCTGTAGTG	(SEQ ID NO 8)
20	MAC-ICG-1 :	CACTCGGTCGATCCGTGTGGA	(SEQ ID NO 9)
25	MIN-ICG-1 :	GCATAGTCCTTAGGGCTGATGCGTT	(SEQ ID NO 12)
30	MIN-ICG-2 :	GCTGATGCGTTCGTCGAAATGTGTA	(SEQ ID NO 13)
35	MIN-ICG-22 :	CTGATGCGTTCGTCGAAATGTGTA	(SEQ ID NO 14)
40	MIN-ICG-222 :	TGATGCGTTCGTCGAAATGTGTA	(SEQ ID NO 15)
45	MIN-ICG-2222 :	GGCTGATGCGTTCGTCGAAATGTGTA	(SEQ ID NO 16)
50	MAL-ICG-1 :	ACTAGATGAACGCGTAGTCCTTGT	(SEQ ID NO 17)
55	MHEF-ICG-1 :	TGGACGAAAACCGGGTGCACAA	(SEQ ID NO 18)
60	MAH-ICG-1 :	GTGTAATTCTTTAACTCTGTGTAAAGTAAGTG	(SEQ ID NO 19)
65	MCO-ICG-11 :	TGGCCGGCGTGTTCATCGAAA	(SEQ ID NO 20)
70	MTH-ICG-11 :	GCACTTCAATTGGTGAAGTGCAGGCC	(SEQ ID NO 21)
75	MTH-ICG-2 :	GCGTGGTCTTCATGGCCGG	(SEQ ID NO 22)
80	MEF-ICG-11 :	ACGCGTGGTCCTCGTGG	(SEQ ID NO 23)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99 provided said probe hybridizes specifically to M. intracellulare strains and MIC-strains.

[0138] The sequences as represented in SEQ ID NO 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99 are new.

[0139] Preferentially, at least two, three, four, five, six, seven, eight or more of said probes are used simultaneously.

[0140] In still another specific embodiment, the invention provides for a method as described above, to detect and identify one or more Mycobacterium intracellulare strains in a sample, wherein step (iii) comprises hybridizing to at least the following probes :

MIN-ICG-1 : GCATAGTCCTTAGGGCTGATGCGTT (SEQ ID NO 12)

50 or to equivalents of said probe,
and/or to any probe derived from SEQ ID NO 89 provided said probe hybridizes specifically to M. intracellulare strains.
[0141] In still another specific embodiment, the invention provides for a method as described above, to detect and identify one or more Mycobacterium scrofulaceum strains in a sample, wherein step (iii) comprises hybridizing to the following probe:

55 MSC-ICG-1 : TCGGCTCGTTCTGAGTGGTGTC (SEQ ID NO 24)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 100 provided said probe hybridizes specifically to M. scrofulaceum.

[0142] The sequence as represented in SEQ ID NO 100 is new.

[0143] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium kansasii strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

10	MKA-ICG-1 :	GATGCGTTGCTACGGGTAGCGT	(SEQ ID NO 25)
	MKA-ICG-2 :	GATGCGTTGCCTACGGGTAGCGT	(SEQ ID NO 26)
	MKA-ICG-3 :	ATGCGTTGCCCTACGGGTAGCGT	(SEQ ID NO 27)
15	MKA-ICG-4 :	CGGGCTCTGTCGAGAGTTGTC	(SEQ ID NO 28)
	MKA-ICG-5 :	CCCTCAGGGATTCTGGGTGTTG	(SEQ ID NO 182)
	MKA-ICG-6 :	GGACTCGTCCAAGAGTGTGTC	(SEQ ID NO 183)
20	MKA-ICG-7 :	TCGGGCTTGGCCAGAGCTGTT	(SEQ ID NO 184)
	MKA-ICG-8 :	GGGTGCGAACAGCAAGCGA	(SEQ ID NO 185)
	MKA-ICG-9 :	GATGCGTTGCCCTACGGG	(SEQ ID NO 186)
25	MKA-ICG-10 :	CCCTACGGTAGCGTGTCTTTG	(SEQ ID NO 187)

and more preferably to:

30	MKA-ICG-3 :	ATGCGTTGCCCTACGGGTAGCGT	(SEQ ID NO 27)
	MKA-ICG-4 :	CGGGCTCTGTCGAGAGTTGTC	(SEQ ID NO 28)
	MKA-ICG-5 :	CCCTCAGGGATTCTGGGTGTTG	(SEQ ID NO 182)
35	MKA-ICG-6 :	GGACTCGTCCAAGAGTGTGTC	(SEQ ID NO 183)
	MKA-ICG-7 :	TCGGGCTTGGCCAGAGCTGTT	(SEQ ID NO 184)
	MKA-ICG-8 :	GGGTGCGAACAGCAAGCGA	(SEQ ID NO 185)
40	MKA-ICG-9 :	GATGCGTTGCCCTACGGG	(SEQ ID NO 186)
	MKA-ICG-10 :	CCCTACGGTAGCGTGTCTTTG	(SEQ ID NO 187)

45 or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 101, 167, 168 or 169 provided said probe hybridizes specifically to M. kansasii.

[0144] The sequences as represented in SEQ ID NO 101, 167, 168 and 169 are new.

[0145] Preferentially, at least two, three or four of said probes are used simultaneously.

[0146] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium chelonae strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

MCH-ICG-1 :	GGTGTGGACTTGACTTCTGAATAG	(SEQ ID NO 29)
MCH-ICG-2 :	CGGCAAAACGTCGGACTGTCA	(SEQ ID NO 30)
5 MCH-ICG-3 :	GGTGTGGTCCTGACTTATGGATAG	(SEQ ID NO 210)

or to equivalents of said probes,
and/or to any probe derived from SEQ ID NO 102, 103 or 174 provided said probe hybridizes specifically to M. chelonae.

10 According to another preferential embodiment, these three probes are used in combination.

[0147] The sequences as represented in SEQ ID NO 102, 103 and 174 are new.

[0148] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium gordonaee strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

MGO-ICG-1 :	AACACCCTCGGGTGCTGTCC	(SEQ ID NO 31)
MGO-ICG-2 :	GTATGCGTTGTCGTCGCGGC	(SEQ ID NO 32)
20 MGO-ICG-5 :	CGTGAGGGGTCATCGTCTGTAG	(SEQ ID NO 33)

and more preferably to:

25 MGO-ICG-5 :	CGTGAGGGGTCATCGTCTGTAG	(SEQ ID NO 33)
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or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 104, 105 or 106 provided said probe hybridizes specifically to M. gordonaee.

30 [0149] The sequences as represented in SEQ ID NO 104 to 106 are new. Preferentially, at least two or three of said probes are used simultaneously.

[0150] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium ulcerans strains or Mycobacterium marinum strains in a sample, wherein step (iii) comprises hybridizing to the following probe:

35 MUL-ICG-1 :	GGTTTCGGGATGTTGTCCCACC	(SEQ ID NO 175)
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or to equivalents of said probe,

40 and/or to any probe derived from SEQ ID NO 157 provided said probe hybridizes specifically to M. ulcerans and M. marinum.

[0151] The sequence as represented in SEQ ID NO 157 is new.

[0152] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium genavense strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

50 MGV-ICG-1 :	CGACTGAGGTCGACGTGGTGT	(SEQ ID NO 176)
MGV-ICG-2 :	GGTGTGTTGAGCATTGAATAGTGGTTGC	(SEQ ID NO 177)
MGV-ICG-3 :	TCGGGCCGCGTGTTCGTCAA	(SEQ ID NO 211)

or to equivalents of said probes,

55 and/or to any probe derived from SEQ ID NO 158, 159, 160, 161 or 162 provided said probe hybridizes specifically to M. genavense.

[0153] The sequences as represented in SEQ ID NO 158 to 162 are new.

[0154] As described in the examples, M. genavense includes M. genavense strains sensu strictu and a group of

closely related strains called M. simiae-like. The former group of strains can be detected specifically with probe MGV-ICG-1 while the latter group hybridizes specifically with probe MGV-ICG-3. Probe MGV-ICG-2 detects both groups.
 [0155] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium xenopi strains in a sample, wherein step (iii) comprises hybridizing to the following probe:

5 MXE-ICG-1 : GTTGGGCAGCAGGCAGTAACC (SEQ ID NO 178)

10 or to equivalents of said probe,
 and/or to any probe derived from SEQ ID NO 163 provided said probe hybridizes specifically to M. xenopi.

[0156] The sequence as represented in SEQ ID NO 163 is new.

15 [0157] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium simiae strains in a sample, wherein step (iii) comprises hybridizing to the following probe:

MSI-ICG-1 : CCGGCAACGGTTACGTGTTC (SEQ ID NO 179)

20 or to equivalents of said probe,
 and/or to any probe derived from SEQ ID NO 164 or 165 provided said probe hybridizes specifically to M. simiae.

[0158] The sequence as represented in SEQ ID NO 164 or 165 is new.

25 [0159] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium fortuitum strains in a sample, wherein step (iii) comprises hybridizing to at least one of the the following probes:

MFO-ICG-1 : TCGTTGGATGGCCTCGCACCT (SEQ ID NO 180)

30 MFO-ICG-2 : ACTTGGCGTGGGATGCGGGAA (SEQ ID NO 181)

or to equivalents of said probes or to any probe derived from SEQ ID NO 166 provided said probe hybridizes specifically to M. fortuitum.

[0160] The sequence as represented in SEQ ID NO 166 is new.

35 [0161] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium celatum strains in a sample, wherein step (iii) comprises hybridizing to the following probe:

40 MCE-ICG-1 : TGAGGGAGCCCGTGCCTGTA (SEQ ID NO 190)

or to equivalents of said probe,

and/or to any probe derived from SEQ ID NO 170 provided said probe hybridizes specifically to M. celatum.

[0162] The sequence as represented in SEQ ID NO 170 is new.

45 [0163] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium haemophilum strains in a sample, wherein step (iii) comprises hybridizing to the following probe:

50 MHP-ICG-1 : CATGTTGGGCTTGATCGGGTGC (SEQ ID NO 191)

or to equivalents of said probe,

and/or to any probe derived from SEQ ID NO 171, 172 or 173 provided said probe hybridizes specifically to M. haemophilum.

[0164] The sequences as represented in SEQ ID NO 171 to 173 are new.

55 [0165] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium malmoense strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

MML-ICG-1 : CGGATCGATTGAGTGCTTGTCCC (SEQ ID NO 188)

MML-ICG-2 : TCTAAATGAACGCAGTGCCGATGG (SEQ ID NO 189)

5

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 107 provided said probe hybridizes specifically to M. malmoense.

[0166] The sequence as represented in SEQ ID NO 107 is new.

[0167] In still another specific embodiment, the invention provides for a method as described above to detect and identify one or more Mycobacterium strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

15 MYC-ICG-1 : ACTGGATAGTGGTTGCGAGCATCTA (SEQ ID NO 1)

MYC-ICG-22 : CTTCTGAATAGTGGTTGCGAGCATCT (SEQ ID NO 2)

or to equivalents of said probes.

20 [0168] According to a preferred embodiment, both probes are used in combination.

[0169] The invention also provides for a method as described above to detect and identify one or more Mycoplasma strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

25 MPN-ICG 1 : ATCGGTGGTAAATTAAACCCAAATCCCTGT (SEQ ID NO 49)

MPN-ICG 2 : CAGTTCTGAAAGAACATTCCGCTTCTTC (SEQ ID NO 50)

MGE-ICG 1 : CACCCATTAATTTTCGGTGTAAAACCC (SEQ ID NO 51)

30 Mycoplasma-ICG : CAAAAGTAAAAACGACAATCTTCTAGTTCC (SEQ ID NO 52)

or to equivalents of said probes,

35 and/or to any probe derived from SEQ ID NO 124 or 125 provided said probe hybridizes specifically with Mycoplasma species.

[0170] Preferentially, at least two, three or four of said probes are used simultaneously.

[0171] More particularly, the invention provides for a method as described above to detect and identify one or more Mycoplasma pneumoniae strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

40

MPN-ICG 1 : ATCGGTGGTAAATTAAACCCAAATCCCTGT (SEQ ID NO 49)

MPN-ICG 2 : CAGTTCTGAAAGAACATTCCGCTTCTTC (SEQ ID NO 50)

45

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 125 provided said probe hybridizes specifically to Mycoplasma pneumoniae. According to a preferred embodiment, both these probes are used in combination.

[0172] The sequence as represented in SEQ ID NO 125 is new.

[0173] In another particular embodiment, the invention provides for a method as described above to detect and identify one or more Mycoplasma genitalium strains in a sample, wherein step (iii) comprises hybridizing to the following probe:

55 MGE-ICG 1 : CACCCATTAATTTTCGGTGTAAAACCC (SEQ ID NO 51)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 124 provided said probe hybridizes specifically to Mycoplasma genitalium.

[0174] The sequence as represented in SEQ ID NO 124 is new.

[0175] The invention also provides for a method as described above to detect and identify one or more Pseudomonas strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

PA-ICG 1 :	TGGTGTGCTGCGTGATCCGAT	(SEQ ID NO 34)
PA-ICG 2 :	TGAATGTTCTGGATGAACATTGATT	(SEQ ID NO 35)
PA-ICG 3 :	CACTGGTGATCATTCAAGTCAAG	(SEQ ID NO 36)
PA-ICG 4 :	TGAATGTTCTGGT(G/A)(G/A)ATGAACATTGATTCTGGTC	(SEQ ID NO 37)
PA-ICG 5 :	CTCTTCACTGGTGATCATTCAAGTCAAG	(SEQ ID NO 38)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 111, 112, 113, 114 or 115 provided said probe hybridizes specifically to Pseudomonas strains.

[0176] The sequences as represented in SEQ ID NO 111 to 115 are new.

[0177] Preferentially, at least two, three or four of said probes are used simultaneously.

[0178] More particularly, the invention provides for a method as described above to detect and identify one or more Pseudomonas aeruginosa strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

PA-ICG 1 :	TGGTGTGCTGCGTGATCCGAT	(SEQ ID NO 34)
PA-ICG 2 :	TGAATGTTCTGGATGAACATTGATT	(SEQ ID NO 35)
PA-ICG 3 :	CACTGGTGATCATTCAAGTCAAG	(SEQ ID NO 36)
PA-ICG 4 :	TGAATGTTCTGGT(G/A)(G/A)ATGAACATTGATTCTGGTC	(SEQ ID NO 37)
PA-ICG 5 :	CTCTTCACTGGTGATCATTCAAGTCAAG	(SEQ ID NO 38)

and most preferably to at least one of the following probes:

PA-ICG 1 :	TGGTGTGCTGCGTGATCCGAT	(SEQ ID NO 34)
PA-ICG 4 :	TGAATGTTCTGGT(G/A)(G/A)ATGAACATTGATTCTGGTC	(SEQ ID NO 37)
PA-ICG 5 :	CTCTTCACTGGTGATCATTCAAGTCAAG	(SEQ ID NO 38)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 111 provided said probe hybridizes specifically to Pseudomonas aeruginosa.

[0179] The sequence as represented in SEQ ID NO 111 is new.

[0180] Preferentially, at least two, three, four or five of said probes are used simultaneously.

[0181] The invention also provides for a method as described above to detect and identify one or more Staphylococcus species in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

STAU-ICG 1 :	TACCAAGCAAAACCGAGTGAATAAAGAGTT	(SEQ ID NO 53)
STAU-ICG 2 :	CAGAAGATGCGGAATAACGTGAC	(SEQ ID NO 54)
5 STAU-ICG 3 :	AACGAAGCCGTATGTGAGCATTGAC	(SEQ ID NO 55)
STAU-ICG 4 :	GAACGTAACCTCATGTTAACGTTGACTTAT	(SEQ ID NO 56)

10 or to equivalents of said probes,
and/or to any probe derived from SEQ ID NO 139, 140, 141, 142, 143 or 144 provided said probe hybridizes specifically
to Staphylococcus species.

[0182] The sequences as represented in SEQ ID NO 139 to 144 are new.

[0183] Preferentially, at least two, three or four of said probes are used simultaneously.

15 [0184] More particularly, the invention provides for a method as described above to detect and identify one or more
Staphylococcus aureus strains in a sample, wherein step (iii) comprises hybridizing to at least one, and preferably both
of the following probes:

20 STAU-ICG 3 :	AACGAAGCCGTATGTGAGCATTGAC	(SEQ ID NO 55)
STAU-ICG 4 :	GAACGTAACCTCATGTTAACGTTGACTTAT	(SEQ ID NO 56)

25 or to equivalents of said probes,
and/or to any probe derived from SEQ ID NO 139, 140, 141, 142 or 143 provided said probe hybridizes specifically to
Staphylococcus aureus. According to a preferred embodiment, both these probes are used in combination.

[0185] In another specific embodiment the invention provides for a method as described above to detect and identify
one or more Staphylococcus epidermidis strains in a sample, wherein step (iii) comprises hybridizing to any probe
derived from SEQ ID NO 144 as long as this probe can be caused to hybridize specifically to Staphylococcus epider-
midis.

[0186] The invention also provides for a method as described above to detect and identify one or more Acinetobacter
strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

35 ACI-ICG 1 :	GCTTAAGTGCACAGTGCTCTAAACTGA	(SEQ ID NO 57)
ACI-ICG 2 :	CACGGTAATTAGTGTGATCTGACGAAG	(SEQ ID NO 58)

40 or to equivalents of said probes,
and/or to any probe derived from SEQ ID NO 126, 127, 128, 129 or 130 provided said probe hybridizes specifically to
Acinetobacter sp.. According to a preferred embodiment, both these probes are used in combination.

[0187] The sequences as represented in SEQ ID NO 126 to 130 are new.

45 [0188] More particularly, the invention provides for a method as described above to detect and identify one or more
Acinetobacter baumanii strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following
probes:

50 ACI-ICG 1 :	GCTTAAGTGCACAGTGCTCTAAACTGA	(SEQ ID NO 57)
ACI-ICG 2 :	CACGGTAATTAGTGTGATCTGACGAAG	(SEQ ID NO 58)

or to equivalents of said probes,
and/or to any probe derived from SEQ ID NO 126 provided said probe hybridizes specifically to Acinetobacter baumanii.
According to a preferred embodiment, both these probes are used in combination.

55 [0189] The invention also provides for a method as described above, to detect and identify one or more Listeria
strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

LIS-ICG 1 : CAAGTAACCGAGAATCATCTGAAAGTGAATC (SEQ ID NO 39)

LMO-ICG 1 : AAACAAACCTTACTTCGTAGAAGTAAATTGGTTAAG

(SEQ ID NO 40)

LMO-ICG 2 : TGAGAGGTTAGTACTTCTCAGTATGTTGTT (SEQ ID NO 41)

LMO-ICG 3 : AGGCACATGCTGAAGCATCGC (SEQ ID NO 42)

LIV-ICG 1 : GTTAGCATAAATAGGTAACATTATGACACAAAGTAAC

(SEQ ID NO 43)

LSE-ICG 1 : AGTTAGCATAAGTAGTGTAACTATITATGACACAAG

LISP-ICG 1 : CGTTTCATAAGCGATCGCACGTT (SEQ ID NO 212)

and most preferably to at least one of the following probes:

LIS-ICG 1 : CAAGTAACCGAGAATCATCTGAAAGTGAATC (SEQ ID NO 39)

LMO-ICG 3 : AGGCACATGCTGAAGCATCGC (SEQ ID NO 42)

LISP-ICG 1 : CGTTTCATAAGCGATCGCACGTT (SEQ ID NO 212)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 116, 118, 119, 120, 121, 213, 214 or 215 provided said probe hybridizes specifically to Listeria species.

[0190] As described in the examples section, Listeria species encompass Listeria species *sensu strictu*, and a group of closely related organisms referred to as "Listeria-like organisms". The latter group can be specifically recognized by probe LISP-ICG 1.

[0191] The sequences as represented in SEQ ID NO 116, 118 to 121 and 213 to 215 are new.

[0192] Preferentially, at least two, three, four, five or six of said probes are used simultaneously.

[0193] More particularly, the invention provides for a method as described above, to detect and identify one or more Listeria monocytogenes strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

LMO-ICG 1 : AAACAAACCTTACTTCGTAGAAGTAAATTGGTTAAG (SEQ ID NO 40)

LMO-ICG 2 : TGAGAGGTTAGTACTTCTCAGTATGTTGTT (SEQ ID NO 41)

LMO-ICG 3 : AGGCACATGCTGAAGCATCGC (SEQ ID NO 42)

and most preferably to the following probe:

LMO-ICG 3 : AGGCACATGCTGAAGCATCGC (SEQ ID NO 42)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 120 provided said probe hybridizes specifically to Listeria monocytogenes.

[0194] Preferentially, at least two, or three of said probes are used simultaneously.

[0195] The invention also provides for a method as described above to detect and identify one or more Brucella strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

BRU-ICG 1 :	CGTGCCGCCCTCGTTCTCTTT	(SEQ ID NO 59)
BRU-ICG 2 :	TTCGCTTCGGGGTGGATCTGTG	(SEQ ID NO 60)
5 BRU-ICG 3 :	GCGTAGTACGCGTTGCGTCGG	(SEQ ID NO 193)
BRU-ICG 4 :	CGCAAGAAGCTTGCTCAAGCC	(SEQ ID NO 194)

and most preferably to at least one of the following probes:

10 BRU-ICG 2 :	TTCGCTTCGGGGTGGATCTGTG	(SEQ ID NO 60)
15 BRU-ICG 3 :	GCGTAGTACGCGTTGCGTCGG	(SEQ ID NO 193)
BRU-ICG 4 :	CGCAAGAAGCTTGCTCAAGCC	(SEQ ID NO 194)

or to equivalents of said probes,

20 and/or to any probe derived from SEQ ID NO 131, 132 or 154 provided said probe hybridizes specifically to Brucella strains.

[0196] The sequences as represented in SEQ ID NO 131, 132 and 154 are new.

[0197] The invention also provides for a method as described above to detect and identify one or more Salmonella strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

25 SALM-ICG 1 :	CAAAACTGACTTACGAGTCACGTTGAG	(SEQ ID NO 61)
SALM-ICG 2 :	GATGTATGCTTCGTTATTCCACGCC	(SEQ ID NO 62)
30 STY-ICG 1 :	GGTCAAACCTCCAGGGACGCC	(SEQ ID NO 63)
SED-ICG 1 :	GCGGTAATGTGTGAAAGCGTTGCC	(SEQ ID NO 64)

and most preferably to the following probe:

35 SALM-ICG 1 :	CAAAACTGACTTACGAGTCACGTTGAG	(SEQ ID NO 61)
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or to equivalents of said probes,

40 and/or to any probe derived from SEQ ID NO 133, 134, 135, 136, 137 or 138 provided said probe hybridizes specifically to Salmonella strains.

[0198] The sequences as represented in SEQ ID NO 133 to 138 are new.

[0199] Preferentially, at least two, three, or four of said probes are used simultaneously.

45 [0200] The invention also relates to a method as described above to detect and identify one or more Chlamydia strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

CHTR-ICG 1 :	GGAAGAACCTGAGAAGGTTCTGAC	(SEQ ID NO 45)
50 CHTR-ICG 2 :	GCATTATATGTAAGAGCAAGCATTCTATTCA	(SEQ ID NO 46)
CHTR-ICG 3 :	GAGTAGCGTGGTGAGGACGAGA	(SEQ ID NO 47)
CHTR-ICG 4 :	GAGTAGCGCGGTGAGGACGAGA	(SEQ ID NO 201)
55 CHPS-ICG 1 :	GGATAACTGTCTTAGGACGGTTGAC	(SEQ ID NO 48)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 122, 123 or 197 provided that said probe hybridizes specifically to Chlamy-

dia strains.

[0201] Preferentially, at least two, three, four or five of said probes are used simultaneously.

[0202] More particularly, the invention relates to a method as described above to detect and identify one or more Chlamydia trachomatis strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

CHTR-ICG 1 :	GGAAGAAGCCTGAGAAGGTTCTGAC	(SEQ ID NO 45)
CHTR-ICG 2 :	GCATTATATGTAAGAGCAAGCATTCTATTCA	(SEQ ID NO 46)
CHTR-ICG 3 :	GAGTAGCGTGGTGAGGACGAGA	(SEQ ID NO 47)
CHTR-ICG 4 :	GAGTAGCGCGGTGAGGACGAGA	(SEQ ID NO 201)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 123 or 197 provided said probe hybridizes specifically to Chlamydia trachomatis.

[0203] The sequences as represented in SEQ ID NO 123 and 197 are new.

[0204] Preferentially, at least two, three or four of said probes are used simultaneously.

[0205] In another particular embodiment, the invention provides for a method as described above to detect and identify one or more Chlamydia psittaci strains in a sample, wherein step (iii) comprises hybridizing to at least the following probe:

CHPS-ICG 1 :	GGATAACTGTCTTAGGACGGTTGAC	(SEQ ID NO 48)
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or to equivalents of said probe,

and/or to any probe derived from SEQ ID NO 122 provided said probe hybridizes specifically to Chlamydia psittaci.

[0206] The sequence of SEQ ID NO 122 is new.

[0207] The invention also provides for a method as described above, to detect one or more Streptococcus strains in a sample, wherein step (iii) comprises hybridizing to any probe derived from SEQ ID NO 145, 146, 147, 148, 149, 150, 151, 152 or 153 provided said probe hybridizes specifically to Streptococcus strains, or equivalents of these probes.

[0208] The sequences as represented in SEQ ID NO 145, 146, 147, 148, 149, 150, 151, 152 or 153 are new.

[0209] The invention also provides for a method as described above, to detect one or more Yersinia enterocolitica strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes :

YEC-ICG 1 :	GGAAAAGGTACTGCACGTGACTG	(SEQ ID NO 198)
YEC-ICG 2 :	GACAGCTGAAACTTATCCCTCCG	(SEQ ID NO 199)
YEC-ICG 3 :	GCTACCTGTTGATGTAATGAGTCAC	(SEQ ID NO 200)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 195 or 196, provided said probe hybridizes specifically to Yersinia enterocolitica.

[0210] The sequences as represented in SEQ ID NO 195 and 196 are new.

[0211] In some cases it may be advantageous to amplify not all organisms present in a sample, but only more specific taxa, which are considered to be relevant. In these cases the invention provides for primers allowing the specific amplification of the spacer region for only those beforehand defined taxa.

[0212] The invention thus provides for a method as described above to detect and identify specifically Chlamydia trachomatis in a sample, wherein step (ii) comprises amplification of the 16S-23S rRNA spacer region or a part of it, using at least one of the following primers:

CHTR-P1 : AAGGTTCTGACTAGGTTGGC (SEQ ID NO 69)
 CHTR-P2 : GGTGAAGTGCTTCATGGATCT (SEQ ID NO 70)

5 or equivalents of these primers, said equivalents differing in sequence from the above mentioned primers by changing one or more nucleotides, provided that said equivalents still amplify specifically the spacer region or part of it from Chlamydia trachomatis.

[0213] Preferably both primers are used.

10 [0214] The invention also provides for a method as described above to detect and identify specifically Listeria species in a sample, wherein step (ii) comprises amplification of the 16S-23S rRNA spacer region or a part of it, using at least one of the following primers:

15	LIS-P1 : ACCTGTGAGTTTCGTTCTCTC	(SEQ ID NO 71)
	LIS-P2 : CTATTGTTCAAGTTTGAGAGGTT	(SEQ ID NO 72)
	LIS-P3 : ATTTCCGTATCAGCGATGATAC	(SEQ ID NO 73)
20	LIS-P4 : ACGAAGTAAAGGTTGTTTCT	(SEQ ID NO 74)
	LIS-P5 : GAGAGGTTACTCTCTTATGTCAG	(SEQ ID NO 75)
	LIS-P6 : CTTTATGTCAGATAAAAGTATGCAA	(SEQ ID NO 202)
25	LIS-P7 : CGTAAAAGGGTATGATTATTTG	(SEQ ID NO 203)

or equivalents of these primers, said equivalents differing in sequence from the above mentioned primers by changing one or more nucleotides, provided that said equivalents still amplify specifically the spacer region or part of it from Listeria species.

30 [0215] The invention also relates to a method as described above to detect and identify specifically Mycobacterium species in a sample, wherein step (ii) comprises amplification of the 16S-23S rRNA spacer region or a part of it, using at least one of the following primers:

35	MYC-P1: TCCCTTGTGGCCTGTGTG	(SEQ ID NO 65)
	MYC-P2: TCCTTCATCGGCTCTCGA	(SEQ ID NO 66)
40	MYC-P3: GATGCCAAGGCATCCACC	(SEQ ID NO 67)
	MYC-P4: CCTCCCACGTCTTCATCG	(SEQ ID NO 68)
45	MYC-P5: CCTGGGTTGACATGCACAG	(SEQ ID NO 192)

or equivalents of these primers, said equivalents differing in sequence from the above mentioned primers by changing one or more nucleotides, provided that said equivalents still amplify specifically the spacer region or part of it from Mycobacterium species.

50 [0216] The invention also provides for a method as described above to detect and identify specifically Brucella species in a sample, wherein step (ii) comprises amplification of the 16S-23S rRNA spacer region or part of it, using at least one of the following primers :

BRU-P1 :	TCGAGAATTGGAAAGAGGTC	(SEQ ID NO 204)
BRU-P2 :	AAGAGGTCGGATTTATCCG	(SEQ ID NO 205)
5 BRU-P3 :	TTCGACTGCAAATGCTCG	(SEQ ID NO 206)
BRU-P4 :	TCTTAAAGCCGCATTATGC	(SEQ ID NO 207)

or equivalents of these primers, said equivalents differing in sequence from the above-mentioned primers by changing one or more nucleotides, provided that said equivalents still amplify specifically the spacer region of part of it from Brucella species.

[0217] The invention also provides for a method as described above to detect and identify specifically Yersinia enterocolitica species in a sample, wherein step (ii) comprises amplification of the 16S-23S rRNA spacer region or part of it, using at least one of the following primers :

YEC-P1 :	CCTAATGATATTGATTGCG	(SEQ ID NO 208)
YEC-P2 :	ATGACAGGTTAACCTTACCCC	(SEQ ID NO 209)

or equivalents of these primers, said equivalents differing in sequence from the above-mentioned primers by changing one or more nucleotides, provided that said equivalents still amplify specifically the spacer region of part of it from Yersinia enterocolitica species.

[0218] The invention also provides for a composition comprising at least one of the probes and/or primers as defined above.

[0219] Said composition may comprise any carrier, support, label or diluent known in the art for probes or primers, more particularly any of the labels or supports detailed in the definitions section.

[0220] The invention relates more particularly to isolated probes and primers as defined above, more particularly any of the probes as specified in Table 1a or any of the primers as specified in Table 1b.

[0221] According to another embodiment, the present invention relates also to new spacer region sequences as defined above and as set out in figures 1-103 (SEQ ID NO 76 to 154, SEQ ID NO 157 to 174, SEQ ID NO 195 to 197 and SEQ ID NO 213 to 215).

[0222] In another embodiment the invention provides for a reverse hybridization method comprising any of the probes as defined above, wherein said probes are immobilized on a known location on a solid support, more preferably on a membrane strip.

[0223] In yet another embodiment the invention provides for a kit for the detection and identification of at least one micro-organism, or the simultaneous detection and identification of several micro-organisms in a sample, comprising the following components:

- 40 (i) when appropriate, at least one suitable primer pair to allow amplification of the intercistronic 16S-23S rRNA spacer region, or a part of it;
- (ii) at least one of the probes as defined above;
- (iii) a buffer, or components necessary to produce the buffer, enabling a hybridization reaction between said probes and the polynucleic acids present in the sample, or the amplified products thereof;
- 45 (iv) a solution, or components necessary to produce the solution, enabling washing of the hybrids formed under the appropriate wash conditions;
- (v) when appropriate, a means for detecting the hybrids resulting from the preceding hybridization.

FIGURE LEGENDS

[0224]

Fig 1: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium tuberculosis strain H37RV ATCC 27294 (SEQ ID NO 76)

55 Fig 2 : represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium avium ATCC 151.769 (ITG 4991) (SEQ ID NO 77)

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Fig 3 : represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium paratuberculosis strains 316F and 2E (SEQ ID NO 78)

Fig 4 : represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 5513 (SEQ ID NO 79)

Fig 5 : represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 8695 (SEQ ID NO 80)

Fig 6 : represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 8708 (SEQ ID NO 81)

Fig 7 : represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 8715 (SEQ ID NO 82)

Fig 8 : represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 8054 (SEQ ID NO 83)

Fig 9 : represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 8737 (SEQ ID NO 84)

Fig 10: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 8743 (SEQ ID NO 85)

Fig 11: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 8745 (SEQ ID NO 86)

Fig 12: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 8748 (SEQ ID NO 87)

Fig 13: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 8752 (SEQ ID NO 88)

Fig 14: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium intracellulare serovar 12 ITG 5915 (SEQ ID NO 89)

Fig 15: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium lufu ITG 4755 (SEQ ID NO 90)

Fig 16: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 5922 (SEQ ID NO 91)

Fig 17: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 1329 (SEQ ID NO 92)

Fig 18: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 1812 (SEQ ID NO 93)

Fig 19: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 5280 (SEQ ID NO 94)

Fig 20: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 5620 (SEQ ID NO 95)

Fig 21: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium strain ITG 5765 (SEQ ID NO 96)

Fig 22: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium ITG 7395 (SEQ

ID NO 97)

Fig 23: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium ITG 8738 (SEQ ID NO 98)

Fig 24: represents the DNA sequence of the 16S-23S rRNA spacer region from Mycobacterium ITG 926 (SEQ ID NO 99)

Fig 25 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium scrofulaceum ITG 4988 (SEQ ID NO 100)

Fig 26: represents the DNA sequence of the 16S-23S spacer region from Mycobacterium kansasii ATCC 22478 (=ITG 4987) (SEQ ID NO 101)

Fig 27 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium chelonae abcessus ITG 4975 (SEQ ID NO 102)

Fig 28: represents the DNA sequence of the 16S-23S spacer region from Mycobacterium chelonae chelonae ITG 9855 (SEQ ID NO 103)

Fig 29: represents the DNA sequence of the 16S-23S spacer region from Mycobacterium ordonae ITG 7703 (SEQ ID NO 104)

Fig 30 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium gordonaiae ITG 7836 (SEQ ID NO 105)

Fig 31: represents the DNA sequence of the 16S-23S spacer region from Mycobacterium gordonaiae ITG 8059 (SEQ ID NO 106)

Fig 32: represents the DNA sequence of the 16S-23S spacer region from Mycobacterium malmoense ITG 4842 and ITG 4832 (SEQ ID NO 107)

Fig 33 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium strain 8757 (SEQ ID NO 108)

Fig 34: represents the DNA sequence of the 16S-23S spacer region from Mycobacterium ITG 8723 (SEQ ID NO 109)

Fig 35: represents the DNA sequence of the 16S-23S spacer region from Mycobacterium ITG 8724 (SEQ ID NO 110)

Fig 36: represents the DNA sequence of the 16S-23S spacer region from Pseudomonas aeruginosa UZG 5669 (SEQ ID NO 111)

Fig 37: represents the DNA sequence of the 16S-23S spacer region from Pseudomonas pseudoalcaligenes LMG 1225 (SEQ ID NO 112)

Fig 38: represents the DNA sequence of the 16S-23S spacer region from Pseudomonas stutzeri LMG 2333 (SEQ ID NO 113)

Fig 39: represents the DNA sequence of the 16S-23S spacer region from Pseudomonas alcaligenes LMG 1224 (SEQ ID NO 114)

Fig 40 : represents the DNA sequence of the 16S-23S spacer region from Pseudomonas putida LMG 2232 (SEQ ID NO 115)

Fig 41 represents the DNA sequence of the small 16S-23S spacer region from Listeria ivanovii CIP 7842 (SEQ ID NO 116)

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Fig 42: represents the DNA sequence of the small 16S-23S spacer region from Listeria monocytogenes (SEQ ID NO 117)

Fig 43: represents the DNA sequence of the small 16S-23S spacer region from Listeria seeligeri serovar 4A nr. 4268 (SEQ ID NO 118)

Fig 44: represents the partial DNA sequence of the large 16S-23S spacer region from partial sequence of the long spacer region of Listeria ivanovii CIP 7842 (SEQ ID NO 119)

Fig 45: represents the DNA sequence of the large 16S-23S spacer region from Listeria monocytogenes IHE serovar 4B (SEQ ID NO 120)

Fig 46: represents the DNA sequence of the large 16S-23S spacer region from Listeria seeligeri serovar 4A nr. 4268 (SEQ ID NO 121)

Fig 47: represents the DNA sequence of the 16S-23S spacer region from Chlamydia psittaci 6BC (SEQ ID NO 122)

Fig 48: represents the DNA sequence of the 16S-23S spacer region from Chlamydia trachomatis (SEQ ID NO 123)

Fig 49: represents the DNA sequence of the 16S-23S spacer region from Mycoplasma genitalium (U. Gobel) (SEQ ID NO 124)

Fig 50: represents the DNA sequence of the 16S-23S spacer region from Mycoplasma pneumoniae ATCC 29432 (SEQ ID NO 125)

Fig 51: represents the DNA sequence of the 16S-23S spacer region from Acinetobacter baumanii LMG 1041 (SEQ ID NO 126)

Fig 52: represents the DNA sequence of the 16S-23S spacer region from Acinetobacter calcoaceticus LMG 1046 (SEQ ID NO 127)

Fig 53: represents the DNA sequence of the 16S-23S spacer region from Acinetobacter haemolyticus LMG 996 (SEQ ID NO 128)

Fig 54: represents the DNA sequence of the 16S-23S spacer region from Acinetobacter johnsonii LMG 999 (SEQ ID NO 129)

Fig 55: represents the DNA sequence of the 16S-23S spacer region from Acinetobacter junii LMG 998 (SEQ ID NO 130)

Fig 56: represents the DNA sequence of the 16S-23S spacer region from Brucella melitensis NIDO Biovar 1 (SEQ ID NO 131)

Fig 57: represents the DNA sequence of the 16S-23S spacer region from Brucella suis NIDO Biovar 1 (SEQ ID NO 132)

Fig 58: represents the DNA sequence of one of the 16S-23S spacer region from Salmonella dublin (SEQ ID NO 133)

Fig 59: represents the DNA sequence of one of the 16S-23S spacer region from Salmonella dublin (SEQ ID NO 134)

Fig 60: represents the DNA sequence of one of the 16S-23S spacer region from Salmonella enteritidis (SEQ ID NO 135)

Fig 61: represents the DNA sequence of one of the 16S-23S spacer region from Salmonella enteritidis (SEQ ID NO 136)

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Fig 62: represents the DNA sequence of one of the 16S-23S spacer region from Salmonella typhimurium (SEQ ID NO 137)

5 Fig 63: represents the DNA sequence of one of the 16S-23S spacer region from Salmonella typhimurium (SEQ ID NO 138)

Fig 64: represents the DNA sequence of one of the 16S-23S spacer region from Staphylococcus aureus strain UZG 5728 (SEQ ID NO 139)

10 Fig 65: represents the DNA sequence of one of the 16S-23S spacer region from Staphylococcus aureus strain UZG 6289 (SEQ ID NO 140)

Fig 66: represents the DNA sequence of one of the 16S-23S spacer region from Staphylococcus aureus strain UZG 6289 (SEQ ID NO 141)

15 Fig 67: represents the DNA sequence of one of the 16S-23S spacer region from Staphylococcus aureus strain UZG 6289 (SEQ ID NO 142)

Fig 68: represents the DNA sequence of one of the 16S-23S spacer region from Staphylococcus aureus strain UZG 6289 (SEQ ID NO 143)

20 Fig 69: represents the DNA sequence of one of the 16S-23S spacer region from Staphylococcus epidermidis strain UZG CNS41 (SEQ ID NO 144)

Fig 70: represents the DNA sequence of the 16S-23S spacer region from Streptococcus mitis UZG 2465 (SEQ ID NO 145)

25 Fig 71: represents the DNA sequence of the 16S-23S spacer region from Streptococcus pyogenes UZG 3671 (SEQ ID NO 146)

Fig 72: represents the DNA sequence of the 16S-23S spacer region from Streptococcus sanguis UZG 1042 (SEQ ID NO 147)

30 Fig 73: represents the DNA sequence of the 16S-23S spacer region from Streptococcus saprophyticus UZG CNS46 (SEQ ID NO 148)

Fig 74: represents the DNA sequence of the 16S-23S spacer region from Streptococcus species UZG 536 (84) (SEQ ID NO 149)

35 Fig 75: represents the DNA sequence of the 16S-23S spacer region from Streptococcus species UZG 4341 (SEQ ID NO 150)

Fig 76: represents the DNA sequence of the 16S-23S spacer region from Streptococcus species UZG 457 (44B) (SEQ ID NO 151)

40 Fig 77: represents the DNA sequence of the 16S-23S spacer region from Streptococcus species UZG 97A (SEQ ID NO 152)

Fig 78: represents the DNA sequence of the 16S-23S spacer region from Streptococcus species UZG 483 (76) (SEQ ID NO 153)

45 Fig 79: represents the DNA sequence of the 16S-23S spacer region from Brucella abortus NIDO Tulya biovar 3 (SEQ ID NO 154)

Fig 80: represents the DNA sequence of the 16S-23S spacer region from Mycobacterium ulcerans ITG 1837 and Mycobacterium marinum ITG 7732 (SEQ ID NO 157)

50 Fig 81: represents the DNA sequence of the 16S-23S spacer region from Mycobacterium genavense ITG 8777

(SEQ ID NO 158)

Fig 82: represents the DNA sequence of the 16S-23S spacer region from Mycobacterium genavense ITG 92-742 (SEQ ID NO 159)

Fig 83 represents the DNA sequence of the 16S-23S spacer region from Mycobacterium genavense ITG 9500 (SEQ ID NO 160)

Fig 84 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium simiae-like ITG 7379 (SEQ ID NO 161)

Fig 85 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium simiae-like ITG 9745 (SEQ ID NO 162)

Fig 86 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium xenopi ITG 4986 (SEQ ID NO 163)

Fig 87 represents the DNA sequence of the 16S-23S spacer region from Mycobacterium simiae A ITG 4485 (SEQ ID NO 164)

Fig 88 : represents the DNA sequence of the 16S-23S spacer region from Mycobacterium simiae B ITG 4484 (SEQ ID NO 165)

Fig 89: represents the DNA sequence of the 16S-23S spacer region from Mycobacterium fortuitum ITG 4304 (SEQ ID NO 166)

Fig 90: represents the DNA sequence of the 16S-23S spacer region from Mycobacterium kansasii ITG 6328 (SEQ ID NO 167)

Fig 91: represents the DNA sequence of the 16S-23S spacer region from Mycobacterium kansasii ITG 8698 (SEQ ID NO 168)

Fig 92: represents the DNA sequence of the 16S-23S spacer region from Mycobacterium kansasii ITG 8973 (SEQ ID NO 169)

Fig 93: represents the DNA sequence of the 16S-23S spacer region from Mycobacterium celatum ITG 94-123 (SEQ ID NO 170)

Fig 94: represents the DNA sequence of the 16S-23S spacer region from Mycobacterium haemophilum ITG 776 (SEQ ID NO 171)

Fig 95: represents the DNA sequence of the 16S-23S spacer region from Mycobacterium haemophilum ITG 778 (SEQ ID NO 172)

Fig 96: represents the DNA sequence of the 16S-23S spacer region from Mycobacterium haemophilum ITG 3071 (SEQ ID NO 173)

Fig 97: represents the DNA sequence of the 16S-23S spacer region from Mycobacterium chelonae ITG 94-330 and ITG 94-379 (SEQ ID NO 174)

Fig 98: represents the DNA sequence of a 16S-23S spacer region from Yersinia enterocolitica strain P95 (SEQ ID NO 195)

Fig 99: represents the DNA sequence of a 16S-23S spacer region from Yersinia enterocolitica strain P95 (SEQ ID NO 196)

Fig 100: represents the DNA sequence of the 16S-23S spacer region from Chlamydia trachomatis strain SSDZ 94 M 1961 (SEQ ID NO 197)

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Fig 101: represents the DNA sequence of a 16S-23S spacer region from Listeria -like isolate MB 405 (SEQ ID NO 213)

5 Fig 102: represents the DNA sequence of a 16S-23S spacer region from Listeria -like isolate MB 405 (SEQ ID NO 214)

Fig 103: represents the DNA sequence of a 16S-23S spacer region from Listeria -like isolate MB 405 (SEQ ID NO 215)

10 **TABLE LEGENDS**

[0225]

Table 1a: List of all new probes originating from the 16S-23S rRNA spacer region

15 Table 1b: List of possible primers to be used for taxon-specific amplification of the spacer region or part of it.

Table 2: Hybridization results for Pseudomonas

20 Table 3: Different probe patterns obtained for mycobacterial strain-types

Table 4: Mycobacteria strains tested in LiPA

25 Table 5: Hybridization results for Listeria (Probes LMO1, 2, LSE1, LIV1, LIS1)

Table 6: Hybridization results for Listeria (Probes LMO3, LIS1)

Table 7: Hybridization results for Chlamydia

30 Table 8: New mycobacterial probes and hybridization results

Table 9: Hybridization results for Brucella

35 Table 10: Hybridization results for Staphylococcus

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Table 1a

	<u>PROBE</u>	<u>SEQUENCE</u>	<u>SEQ ID NO</u>
5	MYC-ICG-1	: ACTGGATAGTGGTGCAGCATCTA	1
	MYC-ICG-22	: CTTCTGAATAGTGGTGCAGCATCT	2
	MTB-ICG-1	: GGGTGCATGACAACAAAGTGGCCA	3
10	MTB-ICG-2	: GACTTGTCCAGGTGTTGCCAC	4
	MTB-ICG-3	: CGGCTAGCGGTGGCGTGTCT	5
	MAI-ICG-1	: CAACAGCAAATGATTGCCAGACACAC	6
15	MIL-ICG-11	: GAGGGGTTCCCGTCTGTAGTG	7
	MIL-ICG-22	: TGAGGGGTTCTCGTCTGTAGTG	8
	MAC-ICG-1	: CACTCGGTGATCCGTGTGGA	9
20	MAV-ICG-1	: TCGGTCCCGTCGTGTGGAGTC	10
	MAV-ICG-22	: GTGGCCGGCGTTATCGAAA	11
	MIN-ICG-1	: GCATAGTCCTAGGGCTGATGCGTT	12
25	MIN-ICG-2	: GCTGATGCGTTCGTCGAAATGTGTA	13
	MIN-ICG-22	: CTGATGCGTTCGTCGAAATGTGT	14
	MIN-ICG-222	: TGATGCGTTCGTCGAAATGTGT	15
30	MIN-ICG-2222	: GGCTGATGCGTTCGTCGAAATGTGTA	16
	MAL-ICG-1	: ACTAGATGAACCGCGTAGTCCTTGT	17
	MHEF-ICG-1	: TGGACGAAAACCGGGTGCACAA	18
35	MAH-ICG-1	: GTGTAATTCTTTAACTCTGTGTAAAGTAAGTG	19
	MCO-ICG-11	: TGGCCGGCGTGTTCATCGAAA	20
	MTH-ICG-11	: GCACTTCAATTGGTGAAGTGCAGGCC	21
40	MTH-ICG-2	: GCGTGGTCTTCATGGCCGG	22
	MEF-ICG-11	: ACGCGTGGTCCTCGTGG	23
	MSC-ICG-1	: TCGGCTCGTTCTGAGTGGTGT	24
45	MKA-ICG-1	: GATGCGTTGCTACGGGTAGCGT	25
	MKA-ICG-2	: GATGCGTTGCCTACGGGTAGCGT	26
	MKA-ICG-3	: ATGCGTTGCCCTACGGGTAGCGT	27
50	MKA-ICG-4	: CGGGCTCTGTTGAGAGTTGT	28
	MCH-ICG-1	: GGTGTGGACTTGACTTCTGAATAG	29
55	MCH-ICG-2	: CGGCAAAACGTCGGACTGTCA	30

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	MCH-ICG-3	:	GGTGTGGTCCTGACTTATGGATAG	210
5	MGO-ICG-1	:	AACACCCTCGGGTGCTGTCC	31
	MGO-ICG-2	:	GTATGCGTTGTCGTCGCGGC	32
	MGO-ICG-5	:	CGTAGGGGTCATCGTCTGTAG	33
10	MUL-ICG-1	:	GGTTTCGGGATGTTGTCCCACC	175
	MGV-ICG-1	:	CGACTGAGGTCGACGTGGTGT	176
	MGV-ICG-2	:	GGTGTGAGCATTGAATAGTGGTTGC	177
	MGV-ICG-3	:	TCGGGCCGCGTGTTCGTAAA	211
15	MXE-ICG-1	:	GTTGGGCAGCAGGCAGTAACC	178
	MSI-ICG-1	:	CCGGCAACGGTTACGTGTTTC	179
	MFO-ICG-1	:	TCGTTGGATGGCCTCGCACCT	180
20	MFO-ICG-2	:	ACTTGGCGTGGGATGCGGGAA	181
	MKA-ICG-5	:	CCCTCAGGGATTTCTGGGTGTTG	182
	MKA-ICG-6	:	GGACTCGTCCAAGAGTGTGTTGCC	183
25	MKA-ICG-7	:	TCGGGCTTGGCCAGAGCTGTT	184
	MKA-ICG-8	:	GGGTGCGAACAGCAAGCGA	185
	MKA-ICG-9	:	GATGCGTTGCCCTACGGG	186
30	MKA-ICG-10	:	CCCTACGGGTAGCGTGTCTTTG	187
	MML-ICG-1	:	CGGATCGATTGAGTGCTTGTCCC	188
	MML-ICG-2	:	TCTAAATGAACGCACTGCCGATGG	189
35	MCE-ICG-1	:	TGAGGGAGCCCGTGCCTGTA	190
	MHP-ICG-1	:	CATGTTGGGCTTGATCGGGTGC	191
	PA-ICG 1	:	TGGTGTGCTCGTGATCCGAT	34
40	PA-ICG 2	:	TGAATGTTCGTGGATGAACATTGATT	35
	PA-ICG 3	:	CACTGGTGATCATTCAAGTCAAG	36
	PA-ICG 4	:	TGAATGTTCGT(G/A)(G/A)ATGAACATTGATTCTGGTC	37
45	PA-ICG 5	:	CTCTTCACTGGTGATCATTCAAGTCAAG	38
	LIS-ICG 1	:	CAAGTAACCGAGAACATCATCTGAAAGTGAATC	39
	LMO-ICG 1	:	AAACAACCTTACTTCGTAGAAGTAAATTGGTTAAG	40
50	LMO-ICG 2	:	TGAGAGGTTAGTACTTCTCAGTATGTTGTTC	41
	LMO-ICG 3	:	AGGCACATGCTGAAGCATCGC	42
	LIV-ICG 1	:	GTTAGCATAAATAGGTAACATTATGACACAAGTAAC	43
55	LSE-ICG 1	:	AGTTAGCATAAGTAGTGTAACTATTATGACACAAG	44

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LISP-ICG 1	:	CGTTTCATAAGCGATCGCACGTT	212
CHTR-ICG 1	:	GGAAGAAGCCTGAGAAGGTTCTGAC	45
5 CHTR-ICG 2	:	GCATTTATATGTAAGAGCAAGCATTCTATTCA	46
CHTR-ICG 3	:	GAGTAGCGTGGTGAGGACGAGA	47
10 CHPS-ICG 1	:	GGATAACTGTCTTAGGACGGTTGAC	48
MPN-ICG 1	:	ATCGGTGGTAAATTAAACCCAAATCCCTGT	49
MPN-ICG 2	:	CAGTTCTGAAAGAACATTCCGCTTCTTC	50
15 MGE-ICG 1	:	CACCCATTAATTTTCGGTGTAAAACCC	51
Mycoplasma-ICG	:	CAAAACTGAAAACGACAATCTTCTAGTTCC	52
STAU-ICG 1	:	TACCAAGCAAAACCGAGTGAATAAAGAGTT	53
20 STAU-ICG 2	:	CAGAAGATGCGGAATAACGTGAC	54
STAU-ICG 3	:	AACGAAGCCGTATGTGAGCATTGAC	55
STAU-ICG 4	:	GAACGTAACTTCATGTTAACGTTGACTTAT	56
25 ACI-ICG 1	:	GCTTAAGTGCACAGTGCTCTAAACTGA	57
ACI-ICG 2	:	CACGGTAATTAGTGTGATCTGACGAAG	58
BRU-ICG 1	:	CGTGCCGCCCTCGTTCTCTTT	59
30 BRU-ICG 2	:	TTCGCTTCGGGGTGGATCTGTG	60
BRU-ICG 3	:	GCGTAGTAGCGTTGCGTCGG	193
35 BRU-ICG 4	:	CGCAAGAAGCTTGCTCAAGCC	194
SALM-ICG 1	:	CAAAACTGACTTACGAGTCACGTTGAG	61
SALM-ICG 2	:	GATGTATGCTTCGTTATTCCACGCC	62
40 STY-ICG 1	:	GGTCAAACCTCCAGGGACGCC	63
SED-ICG 1	:	GCGGTAATGTGTGAAAGCGTTGCC	64
YEC-ICG 1	:	GGAAAAGGTACTGCACGTGACTG	198
45 YEC-ICG 2	:	GACAGCTGAAACTATCCCTCCG	199
YEC-ICG 3	:	GCTACCTGTTGATGTAATGAGTCAC	200
CHTR-ICG 4	:	GAGTAGCGCAGTGAGGACGAGA	201

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Table 1b

<u>PRIMERS</u>	<u>SEQUENCE</u>	<u>SEQ ID NO</u>	
5			
MYC-P1	: TCCCTTGTGGCCTGTGTG	65	
10	MYC-P2	: TCCTTCATCGGCTCTCGA	66
MYC-P3	: GATGCCAAGGCATCCACC	67	
15	MYC-P4	: CCTCCCACGTCCCTCATCG	68
MYC-P5	: CCTGGGTTTGACATGCACAG	192	
20			
CHTR-P1	: AAGGTTTCTGACTAGGTTGGC	69	
CHTR-P2	: GGTGAAGTGCTTGCATGGATCT	70	
25			
LIS-P1	: ACCTGTGAGTTTCGTTCTTCTC	71	
LIS-P2	: CTATTGTTCAAGTTTGAGAGGTT	72	
LIS-P3	: ATTTCCGTATCAGCGATGATAAC	73	
30	LIS-P4	: ACGAAGTAAAGGTTTTTCT	74
LIS-P5	: GAGAGGTTACTCTCTTTATGTCAG	75	
LIS-P6	: CTTTATGTCAGATAAAAGTATGCAA	202	
35	LIS-P7	: CGTAAAAGGGTATGATTATTTG	203
BRU-P1	: TCGAGAATTGGAAAGAGGGTC	204	
40	BRU-P2	: AAGAGGTCGGATTATCCG	205
BRU-P3	: TTCGACTGCAAATGCTCG	206	
BRU-P4	: TCTTAAAGCCGCATTATGC	207	
45			
YEC-P1	: CCTAATGATATTGATTGCG	208	
YEC-P2	: ATGACAGGTTAACCTTACCCC	209	
50			

EXAMPLE 1 : Pseudomonas aeruginosa

[0226] Pseudomonas aeruginosa is a significant human pathogen, usually in the context of serious underlying disease. It is also a major cause of nosocomial infections, which are characteristically prone to resistance to antimicrobial agents. This gram-negative, nonfermentative rod can be responsible for different clinical manifestations, like wound infections, bacteremia, respiratory and urinary tract infections, and is also a major cause of morbidity and mortality in patients with cystic fibrosis.

[0227] Pseudomonas species are currently differentiated based on growth characteristics and several biochemical

features implying a time schedule of 24h to 72h to get a correct identification of the pathogen.

[0228] Already the development of monoclonal or polyclonal antibodies significantly improved the identification of Pseudomonas species. Recently however it has been shown that it is possible to detect organisms directly in clinical samples on a very sensitive and specific way using DNA probes with or without a prior amplification of the target DNA.

[0229] DNA probes to study Pseudomonas aeruginosa are already described and are mainly used for epidemiological typing (Ogle et al., 1987; Samadpour et al., 1988; McIntosh et al., 1992). However, none of these probes have been derived from the 16S-23S spacer.

[0230] The 16S-23S rRNA gene spacer region and a part of the 23S rRNA gene was amplified with conserved primers (upper primer: TGGGGTGAAGTCGTAACAAGGTA , SEQ ID NO 155; lower primer: CCTTTCCCTCACGGTACTGGT, SEQ ID NO 156) using the polymerase chain reaction for the following species :

- Pseudomonas aeruginosa 5669
- Pseudomonas alcaligenes LMG 1224^T
- Pseudomonas fluorescens LMG 5167
- Pseudomonas putida LMG 2232
- Pseudomonas stutzeri LMG 2333^T
- Pseudomonas pseudoalcaligenes LMG 1225^T

[0231] To facilitate cloning of the obtained amplicons a *Nor*I recognition site was added to the lower primer. After purification and digestion of the fragment with *Nor*I, the amplicon was cloned in a *Eco*RV/*Nor*I digested pBluescript SK⁺ plasmid vector.

[0232] Sequencing of the 16S-23S rRNA gene spacer region was performed according the dideoxy-chain terminating chemistry either using double stranded plasmid DNA combined with primers located in the plasmid vector or directly on the PCR products after purification combined with internal PCR primers.

[0233] Fig. 36 to 40 represent the nucleotide sequence of the 16S-23S rRNA gene spacer regions from the different Pseudomonas species described above. For P. fluorescens only partial sequence information was obtained.

[0234] From the nucleic acid sequence of the spacer from P. aeruginosa strain 5669 five oligonucleotide-probes were chosen and chemically synthetized. The sequences of the oligonucleotides are the following:

PA1 = PA-ICG 1 : TGGTGTGCTGCCGTGATCCGATA
 PA2 = PA-ICG 2 : TGAATGTTCGTGGATAACATTGATT
 PA3 = PA-ICG 3 : CACTGGTGATCATTCAAGTCAAG

[0235] Specificity and sensitivity testing of the oligonucleotide-probes was carried out using a reverse hybridization assay. Genomic DNA of the different bacteria tested was amplified using biotinylated primers (idem primers as for cloning procedure, see above). The obtained amplicon, spanning the 16S-23S rRNA gene spacer region, was denatured and hybridized to a membrane-strip onto which the different oligonucleotide probes were immobilized in a line-wise fashion (LiPA). Hybridization was carried out in a mixture of 3xSSC (1xSSC = 0.15 M NaCl, 0.015 M sodium citrate, pH 7.0) and 20% formamide (FA) at a temperature of 50° C for one hour. Washing was done in the same mixture at the same temperature for 15 min.

[0236] Hybrids were detected using a streptavidine conjugate coupled to alkaline phosphatase and the probes were visualized through a precipitation reaction using NBT (nitrobluetetrazolium) and BCIP (bromo-chloro-indolylphosphate).

[0237] The hybridization results obtained with probes PA1, PA2 and PA3 are given in table 4 and show that probes PA1 and PA3 were 100% specific for Pseudomonas aeruginosa and hybridized to all the strains tested. The hybridization signal with probe PA3 at 50° C was not optimal, so the oligonucleotide-probe was improved by adding some additional nucleotides to the specific probe. This newly designed probe is PA5.

PA5 = PA-ICG 5 : CTCTTCACTGGTGATCATTCAAGTCAAG

[0238] Hybridization experiments with probe PA5 proved that this probe also shows a 100% specificity and 100% sensitivity for P. aeruginosa.

[0239] Oligonucleotide-probe PA2 hybridized only to 5 out of 17 P. aeruginosa strains tested. Direct sequencing of the 16S-23S rRNA gene spacer region of the strains which did not hybridize to these probes, showed some hetero-

geneity between different strains. Two mismatches were seen in comparison to the first developed PA2 probe. To overcome this heterogeneity between different strains in the region of probe PA2 a new probe PA4 was designed. This probe is degenerated at the position of the mismatches and some additional nucleotides were added to improve the hybridization signal at 50° C.

5

PA4 = PA-ICG 4 : TGAATGTTCGT(G/A)(G/A)ATGAACATTGATTCTGGTC

[0240] A 100% specificity and 100% sensitivity was obtained with this degenerated probe as is shown by the hybridization results.

10 15 20 25 30 35 40 45 50 55 Table 2 :

Hybridization results for <i>Pseudomonas</i>						
	(n/m: number of strains positive/number of strains tested)					
	taxa tested	PA1	PA2	PA3	PA4	PA5
	<u><i>Pseudomonas aeruginosa</i></u>	17/17	5/17	17/17	17/17	17/17
	<u><i>Pseudomonas alcaligenes</i></u>	0/1	0/1	0/1	0/1	0/1
	<u><i>Pseudomonas fluorescens</i></u>	0/1	0/1	0/1	0/1	0/1
	<u><i>Pseudomonas putida</i></u>	0/1	0/1	0/1	0/1	0/1
	<u><i>Pseudomonas pseudoalcaligenes</i></u>	0/1	0/1	0/1	0/1	0/1
	<u><i>Pseudomonas stutzeri</i></u>	0/1	0/1	0/1	0/1	0/1
	<u><i>Pseudomonas cepacia</i></u>	0/1	0/1	0/1	ND	ND
	<u><i>Neisseria gonorrhoeae</i></u>	0/1	0/1	0/1	ND	ND
	<u><i>Escherichia coli</i></u>	0/1	0/1	0/1	ND	ND
	<u><i>Bordetella pertussis</i></u>	0/1	0/1	0/1	ND	ND
	<u><i>Bordetella parapertussis</i></u>	0/1	0/1	0/1	ND	ND
	<u><i>Bordetella bronchiseptica</i></u>	0/1	0/1	0/1	ND	ND
	<u><i>Mycobacterium tuberculosis</i></u>	0/1	0/1	0/1	ND	ND
	<u><i>Mycobacterium avium</i></u>	0/1	0/1	0/1	ND	ND
	<u><i>Moraxella catarrhalis</i></u>	0/4	0/4	0/4	ND	ND
	<u><i>Haemophilus influenzae</i></u>	0/2	0/2	0/2	ND	ND
	<u><i>Streptococcus pneumoniae</i></u>	0/3	0/3	0/3	ND	ND
	<u><i>Acinetobacter calcoaceticus</i></u>	0/1	0/1	0/1	ND	ND
	<u><i>Staphylococcus aureus</i></u>	0/2	0/2	0/2	ND	ND

EXAMPLE 2: *Mycobacterium*

[0241] A variety of mycobacterial species may be involved in serious human infectious disease. Notorious examples are *Mycobacterium tuberculosis* and *Mycobacterium leprae*. Recently other species such as *M. avium*, *M. intracellulare* and *M. kansasii* have been more frequently encountered as human pathogens especially in immunocompromised hosts.

[0242] Consequently, laboratory diagnosis of mycobacterial infections should not be restricted to the *M. tuberculosis* complex but should ideally include most other clinically relevant mycobacterial species.

[0243] The identification and differentiation of pathogenic mycobacteria at the species level by conventional laboratory techniques is, in general, difficult and time-consuming.

[0244] To overcome these problems DNA-techniques were implemented. The techniques described extended from straightforward DNA-probing to automated sequence analysis. Several approaches have been recently reported (Jonas et al., 1993; Frothingham and Wilson, 1993; Tomioka et al., 1993; Saito et al., 1989; Vaneechoutte et al., 1993; Telenti et al., 1993; Böddinghaus et al., 1990).

[0245] However, these methods all have their particular disadvantages, and most of them still rely on culture. Moreover, and most importantly, none of these techniques allows for a simultaneous detection of the different clinically relevant mycobacterial species in a single test run. Besides, the differentiation of particular groups within the *Mycobacterium aviumintracellulare* complex is problematic and often even impossible.

[0246] To overcome the above-mentioned disadvantages, a LiPA-test was developed which allows for the simultaneous and reliable detection and differentiation of a number of *Mycobacterium* species and groups. The sets of probes used to achieve these goals were all derived from the 16S-23S rRNA spacer region. The methods used are analogous to those mentioned in example 1.

5 [0247] The 16S-23S rRNA spacer region, and part of the 16S and 23S rRNA flanking genes, was amplified by PCR with primers conserved for the genus *Mycobacterium*. At least one of the following primers located in the 16S gene were used as upper primers:

10 MYC-P1: TCCCTTGTGGCCTGTGTG (SEQ ID NO 65)
 MYC-P5: CCTGGGTTTGACATGCACAG (SEQ ID NO 192)

At least one of the following primers, located in the 23S gene, were used as lower primers for the amplification:

15 MYC-P2: TCCTTCATCGGCTCTCGA (SEQ ID NO 66)
 MYC-P3: GATGCCAAGGCATCCACC (SEQ ID NO 67)
 20 MYC-P4: CCTCCCACGTCCATCG (SEQ ID NO 68)

All the above mentioned primers amplified the spacer region of all *Mycobacterium* strains tested, except primer MYC-P2 which was not functional for *M. chelonae*. In order to enhance the sensitivity of the detection, a nested PCR was sometimes carried out, using P5 and P4 as outer primers and P1 and P3 as inner primers.

25 [0248] In order to be able to design and select the probes and probe combinations which fit our purpose, the 16S-23S rRNA spacer region of a number of mycobacterial strains was sequenced. The obtained sequences were compared to each other and to those already known from literature (e.g. Frothingham et al., 1993, 1994; Kampsell et al., 1992; Suzuki et al., 1988; EP-A-0395292; Van der Giessen et al., 1994;) or from publicly accessible data banks. The corresponding sequences are represented in fig.1 to 35 (SEQ ID NO 76 to SEQ ID NO 110).

30 [0249] The probes derived from these data were all adjusted in such a way that the desired hybridization-behaviour was obtained using unified hybridization and wash conditions (i.e. 3xSSC, 20% deionized formamide, 50°C). The set of adjusted probes used for hybridization to different mycobacterial strains is represented in table 1a, SEQ ID NO 1-33. Please note that the probe nomenclature used in this example is an abbreviated version of the one used in table 1a: i.e. the letters "ICG" have always been omitted. According to the specific hybridization pattern obtained, the strains tested could be assigned to one of the following species or species groups: *M. tuberculosis* complex, *M. avium*, *M. intracellulare* or *M. intracellulare* complex, *M. kansasii*, *M. chelonae* and *M. gordonae*. The strains tested which belong to each group are summarized in Table 4. All strains were obtained from the Institute of Tropical Medicine, Antwerp, Belgium. The different probe-patterns obtained for each group are illustrated in Table 3, and are discussed in more detail hereafter.

M. tuberculosis complex

45 [0250] The *M. tuberculosis* complex harbours all strains belonging to *M. tuberculosis*, *M. bovis*, *M. africanum* and *M. microti*. The probes **Mtb1**, **Mtb2** and **Mtb3** hybridize with DNA originating from all *M. tuberculosis* complex strains tested. None of the other strains tested hybridized with these probes at the conditions used.

50 [0251] In addition, *M. tuberculosis* complex strains, as is the case with all other mycobacterial strains tested, hybridize with either the **myc1** or the **myc22** probe or both. The latter two probes are designed as general *Mycobacterium* probes, either alone or in combination with each other.

M. avium/*M. paratuberculosis*

[0252] All *M. avium* and *M. paratuberculosis* strains studied reveal an identical hybridization pattern with the set of probes. For this type of organisms positive hybridization signals are obtained with the probes **myc1/myc22**, **mai1**, **mil11**, **mav1**, **mah1** and **mav22**. The latter two probes hybridize exclusively with *M. avium* and *M. paratuberculosis* strains, and can thus be used as species-specific probes. Since the 16S-23S spacer sequences of *M. avium* isolates and *M. paratuberculosis* isolates are identical or nearly identical these two taxa cannot be discriminated from each other. This finding supports 16S rRNA sequencing data which indicate that *M. avium* and *M. paratuberculosis* should

in fact be considered as belonging to one geno-species (Rogal et al., 1990), *M. avium* ssp. *avium* and *M. avium* ssp. *paratuberculosis*.

M. intracellulare and *M. intracellulare* complex (MIC)

[0253] MIC strains are genotypically highly related organisms, which, according to sequence data of the 16S-23S rRNA spacer region, belong to a distinct cluster which is separate from other *Mycobacterium* species. *M. avium* and *M. scrofulaceum* are their closest relatives. Almost all strains tested which are generally referred to as *M. avium* complex (MAC) strains (the former MAIS-complex) can be found in the MIC group. Thus, the MIC group defined in the current invention encompasses the MAC-type strains described by Frothingham and Wilson (1993) with the exception of MAC-G which appears to be *M. scrofulaceum*. Also *M. intracellulare* strains *sensu stricto* (*M. intracellulare* s.s.) are part of this cluster.

[0254] Because this MIC group contains a quite large group of strains with, among them, subgroups showing different hybridization characteristics to the set of probes, a further subdivision into MIC-types was envisaged.

[0255] Type MIC 1 harbours *M. intracellulare* s.s., together with some other MAC-strains. All MIC 1 type isolates, without exception, hybridize to the following probes: **myc1/myc22, mai1** and **mac1**. The following probes can be used to make further subdivisions within the MIC 1 group : **mil11, min1, min2 to 2222, mil22** and **mhef1**.

[0256] *M. intracellulare* *sensu stricto* strains (type MIC 1.1.a) can be distinguished from other subtypes in this group by virtue of probe **min1** which is positive only for this group of strains. All strains of type MIC 1.1.a strains are positive when tested with the *M. intracellulare* probe of the Gen-Probe Rapid Diagnostic system for MAC.

[0257] Type MIC 1.1.b and MIC 1.2 harbour strains which are highly related to *M. intracellulare*. They can be differentiated by using probes **mil11** and **mil22** (see Table 3). Further subdivision within these groups was not attempted although this could be achieved by using the probes : **min2, min22, min222** and **min2222**. Further subdivision might be of value for epidemiological reasons.

[0258] Only two of our collection of strains tested group as MIC 2 strains. One of these strains is a "Mycobacterium lulu" strain (ITG 4755). The specific probe pattern generated by these strains is characterized by a positive hybridization signal with the following probes : **myc1/myc22, mai1, mi122, mah1** and **mal1**. Variable hybridization results are obtained with probes **min2222, mac1** and **mhef1**. The other probes are negative. It is not unlikely that MIC 2 would eventually prove to be a heterogeneous group when more strains of this type are being identified. The variable probes may help in a further differentiation, if this would become relevant.

[0259] Type MIC 3 groups a fairly high number of MAC-strains which are rather remotely related to *M. intracellulare* s.s. strains and most other MAC-strains. This cluster should be regarded as distinct from *M. avium* and *M. intracellulare* on genotypical grounds. All

[0260] MIC 3 subtypes hybridize to probes **myc1/myc22, mai1, mil22** and **mco1**. A positive signal with the latter probe (mco1) is characteristic for MIC 3 strains. Variable hybridization results are obtained with the following probes : **mac1, mhef1** and **mah1**.

[0261] MIC 3 can be further subdivided into four subtypes by using three probes : **mth11, mth2** and **mef11**. Probe mth2 is specific for type MIC 3.1 which encompasses a group of highly related MAC-strains isolated from immuno-compromised human beings.

[0262] Most MIC 3 strains are located in the MIC 3.1 subtype. Eventually species status may be assigned to this group of strains, as might also be the case for other groups of MAC strains, yet unnamed. In subtypes **MIC 3.4, MIC 3.3** and **MIC 3.2** only two, one and one strain are found respectively in our collection of strains tested.

[0263] Type MIC 4 is a collection of "MAIS" strains (including *M. malmoense*) which are remotely related to *M. intracellulare*. The only probe of the above-described set which hybridizes to MIC 4, apart from the general myc1/myc22 probes, is the **mai1** probe.

[0264] This probe shows a broad specificity, hybridizing also with *M. avium*, *M. intracellulare* and other MIC strains and *M. scrofulaceum*.

M. scrofulaceum

[0265] All *M. scrofulaceum* strains tested reveal an identical hybridization pattern with the set of probes. A positive signal with probe **msc1** is unique to *M. scrofulaceum* strains. The only other probes with a positive signal for this species are evidently myc1/myc22 and also mai1.

M. kansasii

[0266] Probes **mka3** and **mka4** are specific for *M. kansasii*; i.e. a distinct positive signal is obtained on the LiPA strip when amplified DNA from the *M. kansasii* strains is used in the hybridization whilst with all other organisms tested the

signal is absent. Although the sequences of probes **mka1** and **mka2** are not absolutely complementary to the target sequence (3 and 1 mismatches, respectively), these probes also proved to be useful since they hybridized exclusively to *M. kansasi*i DNA and not to any other mycobacterial

5 [0267] DNA tested under the conditions used (50°C, 3xSSC, 20% formamide). This illustrates that probes not necessarily have to match perfectly to the target to be useful, and that modifications in sequence and length may be allowed up to a certain degree.

M. chelonae

10 [0268] The species *M. chelonae* encompasses *M. chelonae* ssp. *chelonae* and *M. chelonae* ssp. *abscessus* strains. The spacer region was sequenced for one strain of each subspecies and small differences were noticed (SEQ ID NO 103 and SEQ ID NO 102). Probes **mch1** and **mch2** hybridize to both strains. All other probes are negative for these 2 strains except for **myc1/myc22**.

15 [0269] Upon testing of probes **mch1** and **mch2** with 2 additional *M. chelonae* strains not mentioned in table 4, i.e. *M. chelonae* 94-379 and *M. chelonae* 94-330, both obtained from the Institute of Tropical Medecine in Antwerp, Belgium, it appeared that they did not hybridize to probe **mch1**. This was confirmed by sequencing the spacer region of these two strains (SEQ ID NO 184). Cluster analysis of the spacer region with other mycobacteria revealed that *M. chelonae* strains can be subdivided in two groups. A third probe **mch3** was designed to specifically detect this second group of strains, to which 94-379 and 94-330 belong.

20 [0270] This illustrates that the use of DNA probes derived from the 16S-23S rRNA spacer region can be helpful in differentiating different groups of strains, which belong to the same species according to the classical identification methods, and possibly can be used to detect and describe new species within the mycobacteria. In this case **mch2** detects all *M. chelonae* strains, whereas **mch1** and **mch3** differentiate between different subgroups.

25 ***M. gordonaie***

[0271] The five *M. gordonaie* strains tested all hybridize to probe **mgo5**. Positive hybridization signals are also obtained with probes **myc1/myc22**, and some *M. gordonaie* strains also hybridize to probes **mgo1** and **mgo2**.

30 **other mycobacterial species**

35 [0272] Strains belonging to other mycobacterial species than those mentioned above only hybridize to the general probes **myc1/myc22**. This indicates that these strains most probably belong to the genus *Mycobacterium*, but do not belong to one of the species or groups which can be specifically identified by using one or more of the other probes described.

[0273] In conclusion we can state that, according to the particular combinations of probes of the invention used, DNA probe tests at different levels can be provided.

40 [0274] When all probes are used in one and the same LiPA-test, differentiation at the species level as well as sub-typing of certain groups of mycobacteria can be achieved. However, the probe-assembly on one strip could be restricted to those probes which are species-specific; in that case identification is performed at the species level. A further reduction of the number of probes on the strip might lead to the specific detection of only one or just a few species. Obviously, LiPA strips can be designed which solely attempt to subtype strains, e.g. those belonging to the *M. intracellulare* complex (MIC). Depending on the particular needs of the laboratoria performing diagnosis and/or typing of mycobacteria, all these different applications might be of value. However, it is clear that by using a combination of probes in a LiPA-format the amount of information obtained as to the identity of the organisms present in the clinical sample, is considerably increased as compared to DNA probe tests using only a single probe. For some groups, or at least for further subdivision of some groups, a single probe uniquely hybridizing to this (sub)group could not be designed. In that case only probe-patterns are able to provide the information needed. For these applications the LiPA is an advantageous format.

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Table 3 : Different probe patterns obtained for mycobacterial (sub)species

Mycobacterium	myc1 myc22	mtb1 mtb2 mtb3	mtb1	mtb1	mav1 mav22	mav1	min1	min222	min2	min2222	min22	mac1
<i>M. tuberculosis</i>	+	+	-	-								
<i>M. bovis</i>	+	-	+	-								
<i>M. avium</i>												
<i>M. paratuberculosis</i>												
MIC 1.1.a	+	-	+	-								
MIC 1.1.b	+	-	+	-								
MIC 1.2	+	-	+	-								
MIC 2	+	-	+	-								
MIC 3.4	+	-	+	-								
MIC 3.3	+	-	+	-								
MIC 3.1	+	-	+	-								
MIC 3.2	+	-	+	-								
MIC 4	+	-	+	-								
<i>M. scrofulaceum</i>												
<i>M. kansasii</i>	+	-										
<i>M. chelonae</i>	+	-										
<i>M. gordonaie</i>	+	-										
<i>Mycobacterium</i> sp.	+	-										

Table 3: continued

Mycobacterium	mco1	mth11	mth2	meff1	mhef1	ma1	msc1	mkal1,2,3,4	mch1,2,3	mgo1,2	mg05
M. tuberculosis	-	-	-	-	-	-	-	-	-	-	-
M. bovis	-	-	-	-	-	-	-	-	-	-	-
M. avium	-	-	-	-	+	-	-	-	-	-	-
M. paratuberculosis	-	-	-	-	-	-	-	-	-	-	-
MIC 1.1.a	-	-	-	-	-	-	-	-	-	-	-
MIC 1.1.b	-	-	-	-	-	-	-	-	-	-	-
MIC 1.2	-	-	-	-	-	-	-	-	-	-	-
MIC 2	-	-	-	-	-	+	-	-	-	-	-
MIC 3.4	+	-	-	-	-	-	-	-	-	-	-
MIC 3.3	+	+	-	-	-	-	-	-	-	-	-
MIC 3.1	+	+	+	-	-	-	-	-	-	-	-
MIC 3.2	+	-	-	-	-	-	-	-	-	-	-
MIC 4	-	-	-	-	-	-	-	-	-	-	-
M. scrofulaceum	-	-	-	-	-	-	-	-	-	-	-
M. kansasii	-	-	-	-	-	-	-	-	-	-	-
M. chelonae	-	-	-	-	-	-	-	-	-	-	-
M. gordoneae	-	-	-	-	-	-	-	-	-	-	-
Mycobacterium sp.	-	-	-	-	-	-	-	-	-	-	-

w : weak / v : very weak / + : + or - , variable according to the strain tested

Table 4

Mycobacteria strains tested in LiPA		
	species/group	strain numbers from Institute of Tropical Medecine Antwerp (except those between parentheses)
5	M. tuberculosis complex	7602, 8004, 8017, 8647, 8872, 9081, 9129, 9173, 9517, (ATCC 27294), 8324, 8428
10	M. avium/ M. paratuberculosis	1101, 1983, 2070, 2074, 4176, 4189, 4191, 4193, 4197, 4204, 4386, 4991, 5872, 5874, 5884, 5887, 5893, 5894, 5897, 5903, 5904, 5905, 5927, 5983, 8180, 8750, (ATCC 25291), <u>M. paratub:</u> (316F), (2E)
15	M. intracellulare (MIC 1.1.a)	4199, 4208, 5701, 5880, 5906, 5908, 5909, 5913, 5915, 5917, 5918, 5920, 5921, 5924, 5925, 5929, 8713, 8717, 8718, 8720, 8721, 8722, 8732, 8740, 8741, 8742, 8744, 8747, 8749
20	MIC 1.1.b	8694, 8745, 8754 8708 5513, 8743 8054, 8190
25	MIC 1.2	8710, 8711, 8712, 8714, 8715, 8716, 8725, 8729, 8733, 8737, 8746, 8751, 8752 5919 8695 8748
30	MIC 2	5922, 4755 (<i>M. lufu</i>)
35	MIC 3.4	1815, 8707
40	MIC 3.3	5620
45	MIC 3.1	925, 926, 1329, 1788, 1794, 1812, 1818, 2069, 2073, 2076, 4541, 4543, 5074, 5280, 5789, 7395, 8739, 8753 8738
50	MIC 3.2	5765
55	M. scrofulaceum	4979, 4988, 5907, 8706, 8726, 8727, 8735, (MB022), (MB023), (MB024)
60	M. kansasii	4987, (ATCC 22478)
65	M. chelonae	4975, 9855
70	M. gordonaee	7703, 7704, 7836, 7838, 8059
75	MIC 4	8723, 8724 8757 4842 (<i>M. malmoense</i>)
80	other mycobacterial species	7732 (<i>M. marinum</i>), 94-123 (<i>M. celatum</i>), 778 (<i>M. haemophilum</i>), 8777 (<i>M. genavense</i>), 4484 (<i>M. siniae</i>), 4986 (<i>M. xenopi</i>), 4304 (<i>M. fortuitum</i>), 1837 (<i>M. ulcerans</i>)

EXAMPLE 3: Listeria

[0275] *Listeria* species are a group of Gram-positive rods widely spread in nature. Within this group it seems that only *L. monocytogenes* is pathogenic to humans and animals. *L. monocytogenes* is the causative agent of listeriosis, giving rise to meningitis, abortions, encephalitis and septicemia. Immunocompromised individuals, newborn infants and pregnant women are high risk groups for this foodborne disease. Most cases have been caused by the consumption of food of animal origin, particularly soft cheeses. Therefore, the presence of *L. monocytogenes* should be excluded from food. For safety measurements, in some countries, the absence of all *Listeria* species is required in food products.

[0276] The classical identification method for *L. monocytogenes* in dairy products involves an enrichment culture for

48 h and subsequently colony forming on selective agar medium for 48 h followed by a whole set of biochemical and morphological assays (Farber and Peterkin, 1991). This procedure could be very much simplified by the use of gene probes.

[0277] Several DNA probes are already described for the identification of L. monocytogenes. Some probes are derived from genes responsible for the pathogenicity of the organism, for instance the listeriolysin O gene (Datta et al., 1993) or the invasion-associated-protein (iap) (Bubert et al., 1992).

[0278] A commercially available identification system, based on a specific 16S rRNA probe, was introduced by Gen-Probe (Herman and De Ridder, 1993; Ninet et al., 1992).

[0279] These specific probes are used as confirmation assays on colonies obtained after enrichment and plating on selective agar medium.

[0280] Recently several publications reported on the use of the polymerase chain reaction to amplify the target region for the DNA probes, which can shorten the time of the assay without interfering with the specificity and the sensitivity of the assay. Different primer sets are described that can specifically amplify L. monocytogenes DNA. These primer sets were derived from the listeriolysin O gene (Golstein Thomas et al., 1991), and the iap gene (Jaton et al., 1992).

[0281] We used the 16S-23S rRNA gene spacer region as the target for the development of a genus-specific probe for Listeria and a probe specific for Listeria monocytogenes.

[0282] Using conserved primers derived from the 3' end of the 16S rRNA and the 5' end of the 23S rRNA (sequences are given in example 1) the spacer region was amplified using the polymerase chain reaction and subsequently cloned in a suitable plasmid vector following the same procedures as in example 3.

[0283] Two amplicons differing in length (800 bp and 1100 bp) were obtained. Both PCR fragments were cloned for the following Listeria species :

- Listeria monocytogenes, serovar 4b, IHE (Instituut voor Hygiene en Epidemiologie, Belgium)
- Listeria ivanovii CIP 78.42 (Collection Nationale de Cultures de Microorganismes de l'Institut Pasteur, France)
- Listeria seeligeri serovar 4a, nr. 42.68 (Bacteriologisches Institut, Südd, Versuchs- und Forschungsanstalt für Milchwirtschaft Weihenstephan, Germany)

[0284] The sequence of the spacer region between the 16S and 23S rRNA gene was determined using the cloned material originating from the 800 bp PCR fragment and this was done for the three described Listeria species. Fig. 41 to 43 show the sequences of the different short spacer regions obtained. The sequence of this short spacer region of L. monocytogenes was also retrieved from the EMBL databank (LMRGSPCR).

[0285] Based on this sequence information, following oligonucleotides for species-specific detection were chosen and chemically synthesized :

LMO-ICG-1 : AAACAAACCTTACTTCGTAGAAGTAAATTGGTTAAG

LMO-ICG-2 : TGAGAGGTTAGTACTTCTCAGTATGTTGTT

LSE-ICG-1 : AGTTAGCATAAGTAGTGTAACATTATGACACAAG

LIV-ICG-1 : GTTAGCATAAATAGGTAACATTATGACACAAAGTAAC

Also, a genus specific probe for Listeria was designed:

LIS-ICG-1 : CAAGTAACCGAGAATCATCTGAAAGTGAATC

The oligonucleotide-probes were immobilized on a membrane strip and following reverse hybridization with biotinylated PCR fragments, the hybrids were visualized using a precipitation reaction. The hybridization results of different Listeria species are summarized in table 5.

Table 5

Species	n	LIS1	LMO1	LMO2	LSE1	LIV1
<u>L. monocytogenes</u>	1	+	+	+	-	-
<u>L. seeligeri</u>	2	+	+	±	+	±
<u>L. ivanovii</u>	3	+	±	-	±	+

Table 5 (continued)

Species	n	LIS1	LMO1	LMO2	LSE1	LIV1
<u>L. welshimeri</u>	3	+	+	±	-	-
<u>L. innocua</u>	2	+	+	+	-	-

[0286] These hybridization results show that probe LIS1 can detect all described Listeria species, but also that the species-specific probes cross-hybridize to each other. Hence, from this short spacer region probes with sufficient specificity could not be found.

[0287] For Listeria monocytogenes the 16S-23S rRNA gene spacer was also determined originating from the 1100 bp fragment. Fig. 45 shows the sequence obtained for this species. This sequence information was also obtained for L. seeligeri (see fig. 46) and partial sequence information of the large spacer region was obtained for L. ivanovii (see fig. 44).

[0288] Based on sequence alignment with L. seeligeri following oligonucleotide-probe was chosen to specifically detect L. monocytogenes.



[0289] Initial hybridization results (not shown) indicated that no cross-hybridization with other Listeria species was seen with this L. monocytogenes probe LMO3, and that all Listeria strains used hybridized to the general probe LIS1.

[0290] The oligonucleotide-probes, LIS1 for detection of all Listeria species and LMO3 for specific detection of L. monocytogenes, were immobilized on a membrane strip and hybridized to labeled amplicons, containing the 16S-23S rRNA spacer region, derived from different organisms. The hybridization results are shown in the following table.

[0291] An excellent specificity and sensitivity were obtained for probes LMO3 and LIS1 respectively at the species and genus level.

Table 6

Taxa tested	n	LIS1	LMO3
<u>Listeria monocytogenes</u>	44	+	+
<u>Listeria ivanovii</u>	10	+	-
<u>Listeria seeligeri</u>	11	+	-
<u>Listeria welshimeri</u>	16	+	-
<u>Listeria innocua</u>	23	+	-
<u>Listeria murrayi</u>	3	+	-
<u>Listeria grayi</u>	2	+	-
<u>Brochotrix thermosphacta</u>	1	-	-
<u>Brochotrix campestris</u>	1	-	-
<u>Bacillus cereus</u>	3	-	-
<u>Bacillus brevis</u>	2	-	-
<u>Bacillus coagulans</u>	1	-	-
<u>Bacillus pumilis</u>	1	-	-
<u>Bacillus macerans</u>	1	-	-
<u>Bacillus lentus</u>	1	-	-
<u>Bacillus firmus</u>	2	-	-
<u>Bacillus subtilis</u>	2	-	-
<u>Bacillus megantum</u>	1	-	-
<u>Enterococcus faecalis</u>	1	-	-
<u>Enterococcus faecium</u>	1	-	-
<u>Enterococcus durans</u>	1	-	-
<u>Lactococcus lactis</u>	3	-	-
<u>Lactococcus casei</u>	1	-	-
<u>Escherichia coli</u>	1	-	-

Table 6 (continued)

Taxa tested	n	LIS1	LMO3
<u>Hafnia halvei</u>	1	-	-
<u>Agrobacterium tumefaciens</u>	2	-	-
<u>Mycoplasma dimorpha</u>	1	-	-
<u>Clostridium tyrobutyricum</u>	1	-	-
<u>Clostridium perfringens</u>	1	-	-
<u>Clostridium sporogenes</u>	1	-	-
<u>Clostridium acetobutylicum</u>	1	-	-
<u>Brucella abortus</u>	1	-	-
<u>Brucella suis</u>	1	-	-
<u>Brucella melitensis</u>	1	-	-
<u>Staphylococcus aureus</u>	1	-	-
<u>Salmonella typhimurium</u>	1	-	-
<u>Salmonella enteritidis</u>	1	-	-
<u>Yersinia enterocolitica</u>	1	-	-

n: number of strains tested

[0292] These two probes can be used for the detection of Listeria species and Listeria monocytogenes directly on food samples or after enrichment of the samples in liquid broth. In both cases amplification problems can occur with the conserved primerset due to the enormous background flora in these samples.

[0293] To circumvent this problem, we designed several sets of primers derived from the 16S-23S rRNA spacer regions of Listeria species.

[0294] Primers LIS-P1 and LIS-P2 are upper primers, whereas LIS-P3 and LIS-P4 are lower primers. These primersets amplify the smaller 16S-23S rRNA spacer region as well as the larger spacer of Listeria species (except L. grayi and L. murrayi). If needed these primers can be used in a nested PCR assay where LIS-P1/LIS-P4 are the outer primers and LIS-P2/LIS-P3 are the inner primers.

[0295] For the specific detection of Listeria monocytogenes probe LMO-ICG-3 was designed and derived from the large 16S-23S rRNA spacer region. In order to specifically amplify only this large spacer region for an improved detection of this pathogen directly in samples a set of primers was derived from the part of sequence information from the large 16S-23S rRNA spacer region that is not present in the smaller rRNA spacer. For this aim, primers LIS-P5 and LIS-P6 are used as the upper primers and LIS-P7 is used as the lower primer.

LIS-P1	:	ACCTGTGAGTTTCGTTCTTCTC	71
LIS-P2	:	CTATTGTTCA GTTTGAGAGGTT	72
LIS-P3	:	ATTTCCGTATCAGCGATGATAC	73
LIS-P4	:	ACGAAGTAAAGGTTGTTTTCT	74
LIS-P5	:	GAGAGGTTACTCTCTTATGTCAG	75
LIS-P6	:	CTTTATGTCAGATAAAGTATGCAA	202
LIS-P7	:	CGTAAAAGGGTATGATTATTG	203

[0296] During the evaluation of the probes for Listeria spp. an organism was isolated from cheese that resembled Listeria according to the classical determination methods. This isolate (MB 405) showed the following characteristics (similar to Listeria spp.): Gram positive, growth on Oxford and Tryptic Soy Agar, catalase positive. The only difference with the Listeria spp. was the motility, which was negative.

[0297] Using the conserved primers as described in example 1 in order to amplify the 16S-23S rRNA spacer region of this isolate MB 405, the same amplicon pattern was obtained with this strain as with Listeria spp. Hybridization of the amplicon showed that there was no signal obtained with any of the probes for Listeria spp.

[0298] Sequencing of the 16S rRNA of isolate MB 405 and subsequent comparison with Listeria spp. and relatives

showed that the organism was more closely related to Listeria spp. than to any other species described in the literature until now. Taxonomical studies will show if this isolate does or does not belong to the genus Listeria. This isolate, and subsequently isolated organisms from the same type, are referred to in this application as Listeria like organisms.

[0299] Isolate MB 405 seemed to contain at least 3 different 16S-23S rRNA spacer regions which were cloned and sequenced. Following alignment with Listeria spp. an oligonucleotide-probe was chosen to specifically detect Listeria-like strains:

LISP-JCG-1 : CGTTTCATAAGCGATCGCACGTT

Reverse hybridization reactions of this probe with the 16S-23S rRNA spacer regions of Listeria spp. showed that there was no cross-hybridization.

EXAMPLE 4: Chlamydia trachomatis

[0300] Chlamydia trachomatis is a small obligate intracellular gram-negative bacterium, which has 15 serovars (A-K, Ba, L1, L2, and L3) distinguished by the major outer membrane protein (MOMP) and contains a cryptic plasmid required for intracellular growth. The A-K and Ba serovars constitute the trachoma biovar, while the L1, L2, and L3 serovars constitute the LGV biovar.

[0301] Serovars A, B, Ba, and C are commonly associated with trachoma, the leading cause of preventable blindness worldwide. The D-K serovars are found mainly in sexually transmitted infections and are the major cause of cervicitis and pelvic inflammatory disease in women, and urethritis and epididymitis in men. Serovars L1, L2 and L3 are involved in lymphogranuloma venereum, a rare sexually transmitted disease.

[0302] Cell culture is regarded as the benchmark method for laboratory diagnosis, although specimen viability is difficult to maintain during transport and laboratory techniques are time-consuming and technically demanding. Therefore, a number of more rapid test kits were developed, such as an enzyme-linked immunosorbent assay, and direct fluorescent-antibody staining. However, none of these immunoassays have been shown to have high levels of sensitivity or specificity.

[0303] A nonisotopic DNA probe assay (Gen-Probe PACE; Woods et al., 1990) that detects chlamydial rRNA is commercially available. Recently, the polymerase chain reaction (PCR) method has been used for detection of Chlamydia infections. Detection was targeted at either the cryptic plasmid (Loeffelholz et al., 1992), or the *omp1* gene, which encodes for the major outer membrane protein (Taylor-Robinson et al., 1992). Compared with other techniques, PCR has higher sensitivity and specificity (Ossewaarde et al., 1992).

None of these assays make use of DNA probes derived from the 16S-23S rRNA gene spacer region.

[0304] For a Chlamydia trachomatis L2 and a Chlamydia psittaci 6BC strain, a part of the ribosomal RNA cistron, containing the 16S-23S rRNA spacer region was amplified using conserved primers (see example 1) and subsequently cloned in a plasmid vector. The 16S-23S rRNA spacer region was sequenced using the dideoxynucleotide terminating chemistry.

[0305] The sequence of the spacer region of both Chlamydia species is shown in fig. 47 to 48.

[0306] Based on this sequence information, following oligonucleotide-probes were chemically synthesized :

CHTR-ICG-1 : GGAAGAACCTGAGAAGGTTCTGAC

CHTR-ICG-2 : GCATTATATGTAAGAGCAAGCATTCTATTCA

CHTR-ICG-3 : GAGTAGCGTGGTGAGGACGAGA

CHPS-ICG-1 : GGATAACTGTCTTAGGACGGTTGAC

[0307] The oligonucleotide-probes were immobilized in a line-wise fashion on a membrane strip and subsequently used in a reverse hybridization assay with biotinylated PCR products, containing the 16S-23S rRNA spacer region, as target.

[0308] Hybridizations were done in a solution of 3xSSC and 20% formamide (FA) at a temperature of 50°C.

[0309] The hybridization results with the different probes are shown in the following table.

Table 7

Strains tested	CHTR1	CHTR2	CHTR3	CHPS1)
<u>Chlamydia trachomatis</u> L2	+	+	+	-
<u>Chlamydia psittaci</u> 6BC	-	-	-	+
<u>Chlamydia psittaci</u> CP	-	-	-	+
<u>Chlamydia psittaci</u> TT	-	-	-	+
<u>Haemophilus ducreyi</u> CIP 542	-	-	-	-
<u>Haemophilus influenzae</u> NCTC 8143	-	-	-	-
<u>Neisseria gonorrhoeae</u> NCTC 8375	-	-	-	-
<u>Moraxella catarrhalis</u> LMG 5128	-	-	-	-
<u>Escherichia coli</u> B	-	-	-	-
<u>Streptococcus pneumoniae</u> S92-2102	-	-	-	-

[0310] As shown in the table at a hybridization temperature of 50°C the probes CHTR1, CHTR2 and CHTR3 are specific for Chlamydia trachomatis and probe CHPS1 is specific for Chlamydia psittaci.

[0311] Several clinical isolates, obtained from the SSDZ, Delft, Netherlands, identified as Chlamydia trachomatis using conventional methods were tested in a reverse hybridization assay with the different oligonucleotide-probes. All Chlamydia trachomatis specific probes gave a positive hybridization signal and none of the isolates reacted with the Chlamydia psittaci probe. For some clinical isolates the CHTR2 probe reacted significantly weaker than CHTR1 or CHTR3. The spacer region of one of these isolates (94 M 1961) was sequenced (SEQ ID NO 197) and the sequence revealed one mismatch with the spacer sequence of strain L2. An additional probe (CHTR4) was derived from this new spacer sequence :

CHTR-ICG-4 : GAGTAGCGCGGTGAGGGACGAGA (SEQ ID NO 201)

[0312] This probe gives a stronger hybridization signal than CHTR2 with some clinical isolates from Chlamydia trachomatis. It can be used alone, or in combination with the CHTR2 probe (e.g. both probes applied in one LiPA-line).

[0313] In order to develop very sensitive assays for the detection of Chlamydia trachomatis directly in clinical specimens a specific primerset was derived from the 16S-23S rRNA spacer region, CHTR-P1 (upper primer) and CHTR-P2 (lower primer), amplifying specifically the spacer region of Chlamydia species.

CHTR-P1	:	AAGGTTCTGACTAGGTTGGC	69
CHTR-P2	:	GGTGAAGTGCTTGCATGGATCT	70

EXAMPLE 6: Mycoplasma pneumoniae and Mycoplasma genitalium

[0314] Mycoplasmas are a group of the smallest prokaryotes known that are able to grow in cell-free media, lack a cell wall, and have very small genomes with a low G+C content. More than 100 different species have been isolated from humans, animals, plants, and insects.

[0315] In humans, mycoplasmas have been recognized either as pathogenic organisms or as commensals. The best known pathogen is Mycoplasma pneumoniae, the causative agent of primary atypical pneumonia, especially in children and young adults. The diagnosis of M. pneumoniae has been based on the direct isolation by the culture method or on the detection of specific antibodies against M. pneumoniae in the patient's serum.

[0316] Another pathogen, first isolated from urethral specimens from patients with nongonococcal urethritis, has been described as Mycoplasma genitalium. This mycoplasma has several properties in common with M. pneumoniae. Both species are pathogenic, and both possess the capability to adhere to erythrocytes, various tissue cells, glass, and plastic surfaces. Furthermore, M. genitalium and M. pneumoniae share antigens, giving rise to extensive cross-reactions in serological tests. The observation that M. genitalium could also be found in respiratory tract specimens from patients with pneumonia and isolated from a mixture with M. pneumoniae has raised questions to the possible pathogenicity of M. genitalium.

[0317] Since cultivation of both species is time-consuming and serology lacks specificity, more rapid and more specific assays were developed to identify these mycoplasmas. The use of hybridization assays with DNA probes was

described for these species, but despite good specificities these tests do not allow the detection of low levels of M. pneumoniae or M. genitalium. So more recently, DNA hybridization techniques were developed using the polymerase chain reaction. M. pneumoniae-specific PCR assays have been reported using the P1 adhesin gene (Buck et al., 1992) and the 16S rRNA gene (Kuppeveld et al., 1992). Specific PCR assays for M. genitalium were described using sequences from the adhesin gene and the 16S rRNA gene.

[0317] The spacer sequences of clinical isolates of M. pneumoniae and M. genitalium (obtained from U. Gobel, University of Freiburg, Germany) were determined. They are shown in fig. 49 to 50. The sequences show some differences to those from other strains of the same species deposited in the EMBL databank (MPMAC and MGG37 respectively). Based on this information four probes were derived: one general Mycoplasma probe, two M. pneumoniae specific, and one M. genitalium specific probe :

Mycoplasma-ICG: CAAAAGTAAAACGACAATCTTCTAGTTCC
 MPN-ICG-1: ATCGGTGGTAAATTAAACCCAAATCCCTGT
 MPN-ICG-2: CAGTTCTGAAAGAACATTCCGCTTCTTC
 MGE-ICG-1: CACCCATTAATTTTCGGTGTAAAACCC

[0318] The probes were applied to LiPA strips and hybridized under standard conditions (3X SSC, 20% formamide at 50°C) to amplified spacer material from four M. pneumoniae strains, one M. genitalium strain and twenty-two non-Mycoplasma species strains. The general probe hybridized only to the five Mycoplasma strains tested, while the specific probes hybridized only to strains of the species for which they were designed.

EXAMPLE 7: Other mycobacterial species

[0319] With the steady improvement of laboratory techniques the information on the systematics and clinical significance of the so called "potentially pathogenic environmental mycobacteria" increased rapidly. With the emergence of newly recognized diseases, additional syndromes associated with different mycobacterial species have emerged and have assumed major importance.

[0320] In order to extend the LiPA test for the simultaneous detection of different mycobacterial species as described in example 2, a new set of DNA probes was designed to specifically identify the following species : Mycobacterium ulcerans, Mycobacterium genavense, Mycobacterium xenopi, Mycobacterium simiae, Mycobacterium fortuitum, Mycobacterium malmoense, Mycobacterium celatum and Mycobacterium haemophilum.

[0321] These probes were derived from the 16S-23S rRNA spacer region sequence. For the above mentioned species this information was obtained through direct sequencing of PCR products or after cloning of the PCR-amplified spacer region. The sequences obtained are represented in fig. 80 to 97, and in fig. 38 for M. malmoense.

[0322] The sequences of the spacer region of the above-mentioned mycobacterial species were compared and aligned to those already described in example 2 or in publicly available sources. From the regions of divergence, species-specific DNA probes were designed. The probes were selected and designed in such a way that the desired hybridization behaviour (i.e. species-specific hybridization) was obtained under the same conditions as those specified for the other mycobacterial probes mentioned in example 2, i.e. 3X SSC, 20% deionized formamide, 50°C. This allows simultaneous detection of at least two, and possibly all, of the mycobacterial species described in the current invention.

[0323] The following oligonucleotide probes were designed from the spacer region sequence of respectively M. ulcerans, M. genavense, M. xenopi, M. simiae, M. fortuitum, M. malmoense, M. celatum and M. haemophilum:

MUL-ICG-1 : GGTTTCGGGATGTTGTCCCACC
 MGV-ICG-1 : CGACTGAGGTCGACGTGGTGT
 MGV-ICG-2 : GGTGTTGAGCATTGAATAGTGGTTGC
 MXE-ICG-1 : GTTGGGCAGCAGGCAGTAACC
 MSI-ICG-1 : GCCGGCAACGGTTACGTGTTTC
 MFO-ICG-1 : TCGTTGGATGGCCTCGCACCT

MFO-ICG-2 : ACTTGGCGTGGGATGCCGGAA
 MML-ICG-1: CGGATCGATTGAGTGCTTGTCCC
 5 MML-ICG-2: TCTAAATGAACGCACTGCCGATGG
 MCE-ICG-1: TGAGGGAGCCCGTGCCTGTA
 10 MHP-ICG-1: CATGTTGGGCTTGATCGGGTGC

[0324] The probes were immobilized on a LiPA strip and hybridized with amplified biotinylated material derived from a set of representative mycobacterial species as described in example 2. Amplification of the spacer region was carried out by PCR using a primer set as described in example 2. The different strains used for specificity testing are shown in table 8 together with the hybridization results obtained. The strains were obtained from the collection of the Institute for Tropical Medicine, Antwerp, Belgium.

[0325] The probes tested (MSI-ICG1, MXE-ICG-1, MFO-ICG-1, MFO-ICG-2, MML-ICG-1, MML-ICG-2, MCE-ICG-1 and MHP-ICG-1) specifically detected M. simiae, M. xenopi, M. fortuitum, M. malmoense, M. celatum and M. haemophilum respectively and showed no cross-hybridization with the other mycobacterial species tested. Thus, these probes allow a specific detection of mycobacterial species which were not further identifiable using the set of DNA probes described in example 2. M. malmoense was classified in example 2 as a "MIC 4"-type, while the other species mentioned above were only hybridizing to the general probes MYC1/MYC22 for the genus Mycobacterium, and were thus classified in example 2 as "other mycobacterial species".

[0326] All tested M. genavense isolates reacted with MGV-ICG1 and MGV-ICG2, and not with MSI-ICG1 designed for M. simiae, closely related to M. genavense. A group of "intermediate" organisms, situated in between M. simiae and M. genavense, were received from the Tropical Institute of Medecine, Antwerp, where they were classified as "M. simiae - like" (strains 4358, 4824, 4833, 4844, 4849, 4857, 4859, 7375, 7379, 7730, 9745, 94-1228). These strains reacted only with probe MGV-ICG2 and not with probe MSI-ICG1 which specifically detects M. simiae strains sensu stricto. Sequencing of the 16S-23S rRNA spacer region of two of these "M. simiae-like" isolates (strains 7379 and 9745) (see SEQ ID NO 161 and 162) confirmed that they were more closely related to M. genavense than to M. simiae. A new probe MGV-ICG3 was designed to specifically detect this group of organisms, which possibly belong to a new species.

MGV-ICG 3 : TCGGGCCGCGTGTTCGTCAAA

[0327] This illustrates again that the use of DNA probes derived from the 16S-23S spacer region can be helpful in differentiating different groups of strains, which are also found indeterminate by classical taxonomic criteria. The use of these DNA probes may possibly lead to the description of new (sub)species within mycobacteria. In this case, the MGV-1 probe would react only with M. genavense strains sensu stricto, MGV-3 probe would react only with the intermediate "M. simiae-like" strains, and MGV-2 probe would detect both types of strains.

[0328] The probe MUL-ICG-1 reacted with all M. ulcerans strains tested, but also showed cross-hybridization with M. marinum strain ITG 7732. Sequencing of the spacer region of this M. marinum strain indeed revealed an identical sequence to that of M. ulcerans strain 1837 (see fig. 80). Further differentiation between M. marinum and M. ulcerans can be done using a probe from the 16S-rRNA gene of M. ulcerans, part of which is co-amplified with the spacer region when primers MYC P1-P5 are used for amplification. A species-specific 16S rRNA probe for M. ulcerans, which can work under the same hybridization conditions as the spacer probes for mycobacterium species differentiation, is for example:

50 TGGCCGGTGCAAAGGGCTG

(SEQ ID NO 216)

[0329] The above paragraph shows that, although it is preferable to use probes derived from the spacer region, it is also possible, and sometimes necessary, to combine the spacer probes with probes derived from other gene sequences, e.g. the 16S rRNA gene. Here again, these additional probes are selected such that they show the desired hybridization characteristics under the same hybridization and wash conditions as the spacer probes.

[0330] For M. kansasii, additional strains to the ones mentioned in example 2 have been tested with probes MKA-ICG-1, 2, 3 and 4 described in example 2. Since none of these probes was entirely satisfactory, additional probes were designed for M. kansasii detection. Therefor, the spacer region of some of the additional M. kansasii strains ITG 6328,

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8698 and 8973 was sequenced (see fig.90 to 92). These strains were also obtained from the Institute of Tropical Medicine in Antwerp, Belgium. Apparently, M. kansasii strains constitute a quite heterogeneous group, with remarkable differences in the spacer sequence between different strains. Additional probes MKA-ICG-5, 6, 7, 8, 9 and 10 were designed, all hybridizing again under the same conditions as those earlier described, i.e. 3X SSC, 20% deionized formamide, 50°C. The probes were tested with a collection of test strains obtained from the Institute of Tropical Medicine, Antwerp, Belgium, and results are shown in table 8.

5 [0331] None of the M. kansasii probes hybridizes with a species other than M. kansasii, as far as tested. However, due to the heterogeneous character of this species, none of the M. kansasii probes hybridizes with all M. kansasii strains. The different M. kansasii probes recognize different strains of M. kansasii. This differential hybridization may 10 be of clinical significance. On the other hand, if detection of all M. kansasii strains is desirable, a combination of different M. kansasii probes can be envisaged.

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Table 8: additional mycobacterial probes

species/type	strain	MUL ICG-1	MGV ICG-1 2 3	MXE ICG-1 2 3	MFO ICG-1 2	MSI ICG-1	MML ICG-1 2	MCE ICG-1	MHP ICG-1
<i>M. tuberculosis</i>	80004	-	-	-	-	-	-	-	-
<i>M. avium</i>	5887	-	-	-	-	-	-	-	-
<i>M. intracellulare</i>	5915	-	-	-	-	-	-	-	-
	5913	-	-	-	-	-	-	-	-
<i>MIC 3.1 strain</i>	1812	-	-	-	-	-	-	-	-
<i>MIC-4 strain</i>	8724	-	-	-	-	-	-	-	-
<i>M. scrofulaceum</i>	4979	-	-	-	-	-	-	-	-
<i>M. kansasii</i>	4987	-	-	-	-	-	-	-	-
	2795	-	-	-	-	-	-	-	-
	6238	-	-	-	-	-	-	-	-
	6362	-	-	-	-	-	-	-	-
	8698	-	-	-	-	-	-	-	-
	8973	-	-	-	-	-	-	-	-
	8974	-	-	-	-	-	-	-	-
	8971	-	-	-	-	-	-	-	-
<i>M. ulcerans</i>	1837	+	-	-	-	-	-	-	-
	3129	+	-	-	-	-	-	-	-
	5114	+	-	-	-	-	-	-	-
	5115	+	-	-	-	-	-	-	-
<i>M. marinum</i>	7732	+	-	-	-	-	-	-	-
<i>M. malmoense</i>	4832	-	-	-	-	-	-	-	++
	4842	-	-	-	-	-	-	-	-
<i>M. gordonaie</i>	7703	-	-	-	-	-	-	-	-

Table 8 continued

M. chelone	4975 9855 94-330 94-379	- - - -						
M. gordoniæ	94-123	-	-	-	-	-	-	-
M. haemophilum	778 3071	-	-	-	-	-	-	-
M. genavense and M. simiae-like	8777 9745 92-742 7379 9500	- - - - +	+ + + + +	- + - + +	- + - + -	- - - - -	- - - - -	- - - - -
M. simiae	4484 4485	- -						
M. xenopi	4986	-	-	-	-	-	-	-
M. fortuitum	4304	-	-	-	-	-	-	-

\rightarrow = negative reaction, \rightarrow = positive reaction, w = weak reaction, \pm = variable reaction, blanc = non tested

Table 8 continued

species/type	strain	MKA ICG-3	MKA ICG-4	MKA ICG-5	MKA ICG-6	MKA ICG-7	MKA ICG-8	MKA ICG-9	MKA- ICG-10
<i>M. tuberculosis</i>	8004	-	-	-	-	-	-	-	-
<i>M. avium</i>	5887	-	-	-	-	-	-	-	-
<i>M. intracellulare</i>	5915 5913	-	-	-	-	-	-	-	-
<i>MIC 3.1 strain</i>	1812	-	-	-	-	-	-	-	-
<i>MIC-4 strain</i>	8724	-	-	-	-	-	-	-	-
<i>M. scrofulaceum</i>	4979	-	-	-	-	-	-	-	-
<i>M. kansassii</i>	4987 2795 6238 6362 8698 8973 8974 8971	+ + + + - - - -	+ - + + - - - -	- - + - - - - -	- - + - - - - -	- - + - - - - -	- - + - - - - -	- - + - - - - -	- - + - - - - -
<i>M. ulcerans</i>	1837 3129 5114 5115								
<i>M. marinum</i>	7732	-	-	-	-	-	-	-	-
<i>M. malmoense</i>	4832 4842	-	-	-	-	-	-	-	-
<i>M. gordongae</i>	7703	-	-	-	-	-	-	-	-

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Table 8 continued

M. cheloneae	4975 9855 94-330 94-379							
M. celatum	94-123							
M. haemophilum	778 3071							
M. genavense and M. simiae-like	8777 9745 92-742 7379 9500							
M. simiae	4484 4485							
M. xenopi	4986							
M. fortuitum	4304							

EXAMPLE 8: Brucella

[0332] Brucellosis is a very widespread and economically important zoonosis which also affects humans.

[0333] For the identification of Brucella spp., mainly bacteriological and immunological detection techniques are being used. These tests are time-consuming and often give falsepositive results. Quick and reliable identification meth-

ods are being developed, mainly based on DNA amplification and hybridization.

[0334] Specific detection of Brucella spp. based on the amplification of a 43 kDa outer membrane protein (Fekete A. et al., 1990) or of a part of the 16S rRNA gene (Herman and De Ridder, 1992) were already described.

[0335] In order to develop specific DNA probes and primers for the detection of Brucella spp. we analyzed the 16S-23S rRNA gene spacer region. Using conserved primers (sequences are given in example 1) the spacer region was amplified and subsequently cloned into the Bluescript SK+ vector following the same procedures as in example 1. The obtained amplicon of about 1400 bp in length was cloned for the following Brucella species: - Brucella abortus NIDO Tulya biovar 3 (SEQ ID NO 154)

- 10 - Brucella melitensis NIDO biovar 1 (SEQ ID NO 131)
- Brucella suis NIDO biovar 1 (SEQ ID NO 132)

*Hind*III digestion of the constructs, followed by subcloning of the obtained fragments (n=3) facilitated the sequencing of the spacer region for the three described Brucella spp..

15 Fig. 56, 57 and 79 represent the sequences of the spacer regions obtained for the above-mentioned strains of respectively Brucella melitensis, Brucella suis and Brucella abortus.

Due to the high homology of these spacer region sequences between different Brucella species, no species-specific DNA probes were deduced from this sequence information, and only genus-specific probes were designed.

[0336] For this purpose, the following probes were chemically synthesized:

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 BRU-ICG 1 : CGTGCCGCCTCGTTCTCTTT
 BRU-ICG 2 : TTTCGCTTCGGGGTGGATCTGTG
 25 BRU-ICG 3 : GCGTAGTAGCGTTGCGTCGG
 BRU-ICG 4 : CGCAAGAAGCTTGCTCAAGCC

30 The oligonucleotides were immobilized on a membrane strip and following reverse hybridization with biotinylated PCR fragments, the hybrids were visualized using a precipitation reaction. The hybridization results of the immobilized probes with different Brucella spp. and related organisms are represented in the table 9.

[0337] These hybridization results show that probes BRU-ICG 2, BRU-ICG 3 and BRU-ICG 4 are specific for Brucella spp. and can be used in a reverse hybridization assay for detection of these pathogens. Probe BRU-ICG 1 cross-hybridizes with Ochrobactrum antropi and Rhizobium loti strains, which are two taxonomically highly related organisms, but which are not expected to be present in the same sample material as used for Brucella detection.

[0338] As described in previous examples (e.g. 3 and 4) also for Brucella specific primers were chosen from the 16S-23S rRNA spacer region, in order to specifically amplify the spacer region from Brucella strains.

[0339] BRU-P1 and BRU-P2 are used as upper primers, while BRU-P3 and BRU-P4 are used as lower primers. When used in a nested PCR assay the combination BRU-P1/BRU-4 is the outer primerset whereas the combination BRU-P2/BRU-P3 is the inner primerset.

BRU-P1	: TCGAGAATTGGAAAGAGGGTC	204
BRU-P2	: AAGAGGTCGGATTATCCG	205
BRU-P3	: TTCAACTGCAAATGCTCG	206
BRU-P4	: TCTTAAAGCCGCATTATGC	207

50 TABLE 9

TAXA TESTED	n	BRU-ICG 1	BRU-ICG 2	BRU-ICG 3	BRU-ICG4
<u>Brucella abortus</u>	6	+	+	+	+
<u>Brucella suis</u>	3	+	+	+	+
<u>Brucella melitensis</u>	4	+	+	+	+

TABLE 9 (continued)

TAXA TESTED	n	BRU-ICG 1	BRU-ICG 2	BRU-ICG 3	BRU-ICG4
<u>Brucella ovis</u>	2	+	+	+	+
<u>Brucella canis</u>	2	+	+	+	+
<u>Brucella neotomae</u>	1	+	+	+	+
<u>Phyllobacterium rubiacearum</u>	1	-	-	NT	NT
<u>Ochrobactrum anthropi</u>	8	+	-	-	-
<u>Agrobacterium tumefaciens</u>	2	-	-	NT	NT
<u>Agrobacterium rhizogenes</u>	1	-	-	NT	NT
<u>Mycoplana dimorpha</u>	1	-	-	NT	NT
<u>Rhizobium loti</u>	1	+	-	-	-
<u>Rhizobium meliloti</u>	1	-	-	NT	NT
<u>Rhizobium leguminosarum</u>	1	-	-	NT	NT
<u>Bradyrhizobium japonicum</u>	1	-	-	NT	NT
<u>Brochothrix thermosphacta</u>	1	-	-	NT	NT
<u>Brochothrix campestris</u>	1	-	-	NT	NT
<u>Bacillus cereus</u>	3	-	-	NT	NT
<u>Bacillus brevis</u>	2	-	-	NT	NT
<u>Bacillus coagulans</u>	1	-	-	NT	NT
<u>Bacillus pumilis</u>	1	-	-	NT	NT
<u>Bacillus macerans</u>	1	-	-	NT	NT
<u>Bacillus lentus</u>	1	-	-	NT	NT
<u>Bacillus firmus</u>	2	-	-	NT	NT
<u>Bacillus subtilis</u>	2	-	-	NT	NT
<u>Bacillus megantum</u>	1	-	-	NT	NT
<u>Enterococcus faecalis</u>	1	-	-	NT	NT
<u>Enterococcus faecium</u>	1	-	-	NT	NT
<u>Enterococcus durans</u>	1	-	-	NT	NT
<u>Lactobacillus lactis</u>	3	-	-	NT	NT
<u>Lactobacillus casei</u>	1	-	-	NT	NT
<u>Leuconostoc lactis</u>	1	-	-	NT	NT
<u>Escherichia coli</u>	1	-	-	NT	NT
<u>Hafnia halvei</u>	1	-	-	NT	NT
<u>Clostridium tyrobutyricum</u>	1	-	-	NT	NT
<u>Clostridium perfringens</u>	1	-	-	NT	NT
<u>Clostridium sporogenes</u>	1	-	-	NT	NT
<u>Clostridium acetobutylicum</u>	1	-	-	NT	NT
<u>Staphylococcus aureus</u>	1	-	-	NT	NT
<u>Salmonella enteritidis</u>	1	-	-	NT	NT
<u>Yersinia enterocolitica</u>	1	-	-	NT	NT
<u>Listeria monocytogenes</u>	1	-	-	NT	NT
<u>Listeria ivanovii</u>	1	-	-	NT	NT
<u>Listeria seeligeri</u>	1	-	-	NT	NT
<u>Listeria welshimeri</u>	1	-	-	NT	NT
<u>Listeria innocua</u>	1	-	-	NT	NT
<u>Listeria murrayi</u>	1	-	-	NT	NT
<u>Listeria grayi</u>	1	-	-	NT	NT

NT = Not tested n = number of strains tested

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EXAMPLE 9: Staphylococcus aureus[0340] *Staphylococcus aureus* is the staphylococcal species most commonly associated with human and animal

infections. *Staphylococcus aureus* strains have been identified as important etiologic agents in both community-acquired and nosocomial infections. Recently nosocomial infection with methicillin-resistant *S. aureus* (MRSA) appear to be increasingly prevalent in many countries. The strains belonging to this species are also causative agents of food spoilage and poisoning.

[0341] In order to discriminate in a fast and specific way *S. aureus* strains from other staphylococci, the use of molecular techniques based on DNA probes and/or PCR were already described in the literature. Examples of target genes used for the development of these DNA based assays are the 16S rRNA gene (De Buyser et al., 1992; Geha et al, 1994), the *mecA* gene (Ubuakata et al., 1992; Shimaoka et al., 1994) and the *nuc* gene (Brakstad et al., 1992; Chesneau et al., 1993).

[0342] As a target for the development of specific DNA probes we chose the 16S-23S rRNA gene spacer region. Amplification using conserved primers derived from the 16S and the 23S rRNA genes (sequences, see example 1) showed that the pattern obtained was not similar in all *S. aureus* strains tested. A lot of variation was seen in either the number of fragments obtained and in the size of these different fragments.

[0343] One spacer region from strain UZG 5728 and four spacer regions (differing in length) from strain UZG 6289 were cloned into Bluescript SK+ vector and subsequently sequenced. The sequences are represented in fig. 64 to fig. 68 (SEQ ID NO 139 to SEQ ID NO 143). For the development of specific DNA probes these different spacer regions were compared to each other and to the spacer region derived from *Staphylococcus epidermidis* strain UZG CNS41 (SEQ ID NO 144).

[0344] The following probes were chemically synthesized:

STAU-ICG 1 : TACCAAGCAAAACCGAGTGAATAAAGAGTT
 STAU-ICG 2 : CAGAAGATGCGGAATAACGTGAC
 STAU-ICG 3 : AACGAAGCCGTATGTGAGCATTGAC
 STAU-ICG 4 : GAACGTAACCTCATGTTAACGTTGACTTAT

[0345] The oligonucleotides were immobilized on a membrane strip and following reverse hybridization with biotinylated PCR fragments, the hybrids were visualized using a colorimetric precipitation reaction.

[0346] The hybridization results of the immobilized probes with different *Staphylococcus* spp. and non-staphylococcal organisms are represented in Table 10.

[0347] These hybridization results show that only probes STAU-ICG 3 and STAU-ICG 4 are specific for *Staphylococcus aureus* strains. Probe STAU-ICG 1 reacts with all *Staphylococcus* spp. tested and probe STAU-ICG 2 cross-hybridizes with the *S. lugdinensis* strain.

Neither probe STAU-ICG 3 nor probe STAU-ICG 4 detects all *S. aureus* strains tested, but when both probes are used simultaneously in a LiPA assay, all *S. aureus* strains tested hybridize with one of these probes or with both.

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Table 10

Strains tested	n	STAU-ICG 1	STAU-ICG 2	STAU-ICG 3	STAU-ICG 4
<i>Staphylococcus aureus</i>	13	+	-	-	-
<i>Staphylococcus aureus</i>	10	+	-	-	-
<i>Staphylococcus aureus</i>	3	+	-	-	-
<i>Staphylococcus aureus</i>	1	-	-	-	-
<i>Staphylococcus epidermidis</i>	11	-	-	-	-
<i>Staphylococcus saprophyticus</i>	1	-	-	-	-
<i>Staphylococcus haemolyticus</i>	1	-	-	-	-
<i>Staphylococcus capitis</i>	1	-	-	-	-
<i>Staphylococcus lugdunensis</i>	1	-	-	-	-
<i>Staphylococcus hominis</i>	1	-	-	-	-
<i>Bordetella pertussis</i>	1	-	-	-	-
<i>Bordetella parapertussis</i>	1	-	-	-	-
<i>Bordetella bronchiseptica</i>	1	-	-	-	-
<i>Mycobacterium tuberculosis</i>	1	-	-	-	-
<i>Mycobacterium avium</i>	1	-	-	-	-
<i>Moraxella catarrhalis</i>	4	-	-	-	-
<i>Haemophilus influenzae</i>	2	-	-	-	-
<i>Streptococcus pneumoniae</i>	3	-	-	-	-
<i>Pseudomonas cepacia</i>	1	-	-	-	-
<i>Pseudomonas aeruginosa</i>	3	-	-	-	-
<i>Acinetobacter calcoaceticus</i>	1	-	-	-	-

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SEQUENCE LISTING

5 (1) GENERAL INFORMATION:

(i) APPLICANT:

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10 15 (ii) TITLE OF INVENTION: SIMULTANEOUS DETECTION, IDENTIFICATION AND DIFFERENTIATION OF EUBACTERIAL TAXA USING A HYBRIDIZATION ASSAY

20 (iii) NUMBER OF SEQUENCES: 216

(iv) COMPUTER READABLE FORM:

- (A) MEDIUM TYPE: Floppy disk
- (B) COMPUTER: IBM PC compatible
- (C) OPERATING SYSTEM: PC-DOS/MS-DOS
- (D) SOFTWARE: PatentIn Release #1.0, Version #1.25 (EPO)

25 (2) INFORMATION FOR SEQ ID NO: 1:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 25 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

30 35 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

ACTGGATAGT GGTTGCGAGC ATCTA

25

45 (2) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

50 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

55 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

CTTCTGAATA GTGGTTGCGA GCATCT

26

5 (2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 25 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

10 (ii) MOLECULE TYPE: cDNA

15 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

GGGTGCATGA CAACAAAGTT GGCCA

25

(2) INFORMATION FOR SEQ ID NO: 4:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 24 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

40 GACTTGTTC AGGTGTTGTC CCAC

24

(2) INFORMATION FOR SEQ ID NO: 5:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

CGGCTAGCGG TGGCGTGTTC T

21

5 (2) INFORMATION FOR SEQ ID NO: 6:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 26 base pairs
 (B) TYPE: nucleic acid
 10 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

15 (iii) ANTI-SENSE: NO

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:

CAACAGCAAA TGATTGCCAG ACACAC

26

(2) INFORMATION FOR SEQ ID NO: 7:

25 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 21 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

35 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

40 GAGGGGTTCC CGTCTGTAGT G

21

(2) INFORMATION FOR SEQ ID NO: 8:

45 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 22 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

50 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

TGAGGGGTTC TCGTCTGTAG TG

22

5 (2) INFORMATION FOR SEQ ID NO: 9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

10 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

15 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

20 CACTCGGTG ATCCGTGTGG A

21

(2) INFORMATION FOR SEQ ID NO: 10:

25 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10:

TCGGTCCGTC CGTGTGGAGT C

21

40 (2) INFORMATION FOR SEQ ID NO: 11:

45 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

50 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:

55 GTGGCCGGCG TTCATCGAAA

20

(2) INFORMATION FOR SEQ ID NO: 12:

5 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 25 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

10 (ii) MOLECULE TYPE: cDNA

 (iii) HYPOTHETICAL: NO

15 (iii) ANTI-SENSE: NO

 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12:

20 GCATAGTCCT TAGGGCTGAT GCGTT

25

(2) INFORMATION FOR SEQ ID NO: 13:

25 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 25 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

 (ii) MOLECULE TYPE: cDNA

30 (iii) HYPOTHETICAL: NO

 (iii) ANTI-SENSE: NO

35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13:

GCTGATGCGT TCGTCGAAAT GTGTA

25

(2) INFORMATION FOR SEQ ID NO: 14:

40 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 23 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: cDNA

 (iii) HYPOTHETICAL: NO

50 (iii) ANTI-SENSE: NO

 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:

55 CTGATGCGTT CGTCGAAATG TGT

23

(2) INFORMATION FOR SEQ ID NO: 15:

5 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

10 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 15:

TGATGCGTTC GTCGAAATGT GT

22

20 (2) INFORMATION FOR SEQ ID NO: 16:

25 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

30

(iii) ANTI-SENSE: NO

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 16:

GGCTGATGCG TTCGTCGAAA TGTGTAA

27

40 (2) INFORMATION FOR SEQ ID NO: 17:

45 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

45

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

50

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 17:

55 ACTAGATGAA CGCGTAGTCC TTGT

24

(2) INFORMATION FOR SEQ ID NO: 18:

5 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

10 (ii) MOLECULE TYPE: cDNA

15 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 18:

TGGACGAAAA CGGGTGCAC AA

22

20 (2) INFORMATION FOR SEQ ID NO: 19:

25 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 38 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

30 (iii) ANTI-SENSE: NO

35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 19:

GTTAAATTTC TTTTTTAACT CTTGTGTGTA AGTAAGTG

38

(2) INFORMATION FOR SEQ ID NO: 20:

40 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

45 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 20:

TGGCCGGCGT GTTCATCGAA A

21

55 (2) INFORMATION FOR SEQ ID NO: 21:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 21:

GCAC TTCAAT TGGTGAAGTG CGAGCC

26

(2) INFORMATION FOR SEQ ID NO: 22:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 19 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 22:

GCGTGCTCTT CATGGCCGG

19

(2) INFORMATION FOR SEQ ID NO: 23:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 18 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

45 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 23:

ACGGCGTGGTC CTTCGTG

18

(2) INFORMATION FOR SEO ID NO: 24:

55

- (A) LENGTH: 22 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 24:

TCGGCTCGTT CTGAGTGGTG TC

??

(2) INFORMATION FOR SEQ ID NO: 25:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 23 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 25:

GATGCGTTG CTACGGGTAG CGT

23

(2) INFORMATION FOR SEQ ID NO: 26:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 23 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 36.

GATGCCTTGC CTAGCCCTAC CCT

23

(3) INFORMATION FOR SEQ ID NO: 23

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs

(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

10 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 27:

15 ATGCGTTGCC CTACGGGTAG CGT

23

(2) INFORMATION FOR SEQ ID NO: 28:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 28:

CGGGCTCTGT TCGAGAGTTG TC

22

(2) INFORMATION FOR SEQ ID NO: 29:

35 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 25 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

45 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 29:

50 GGTGTGGACT TTGACTTCTG AATAG

25

(2) INFORMATION FOR SEQ ID NO: 30:

55 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid

(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10
15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 30:

CGGCAAAACG TCGGACTGTC A

21

(2) INFORMATION FOR SEQ ID NO: 31:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
20 (C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

25 (iii) HYPOTHETICAL: NO
(iii) ANTI-SENSE: NO

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 31:

AACACCCTCG GGTGCTGTCC

20

(2) INFORMATION FOR SEQ ID NO: 32:

35 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

45 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 32:

50 GTATGCGTTG TCGTTCGCGG C

21

(2) INFORMATION FOR SEQ ID NO: 33:

55 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 33:

CGTGAGGGGT CATCGTCTGT AG

22

15

(2) INFORMATION FOR SEQ ID NO: 34:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

20

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

25

(iii) ANTI-SENSE: NO

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 34:

TGGTGTGCTG CGTGATCCGA T

21

(2) INFORMATION FOR SEQ ID NO: 35:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

35

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 35:

TGAATGTTCG TGGATGAACA TTGATT

26

45

(2) INFORMATION FOR SEQ ID NO: 36:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 23 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

50

55

5 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 36:

CACTGGTGAT CATTCAAGTC AAG

23

15 (2) INFORMATION FOR SEQ ID NO: 37:

15 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 33 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: cDNA
(iii) HYPOTHETICAL: NO
25 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 37:

30 TGAATGTTCG TVVATGAACA TTGATTTCTG GTC

33

(2) INFORMATION FOR SEQ ID NO: 38:

35 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 29 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: cDNA
(iii) HYPOTHETICAL: NO
(iii) ANTI-SENSE: NO

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 38:

CTCTTCACT GGTGATCATT CAAGTCAAG

29

50 (2) INFORMATION FOR SEQ ID NO: 39:

55 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 39:

CAAGTAACCG AGAATCATCT GAAAGTGAAT C

31

(2) INFORMATION FOR SEQ ID NO: 40:

15 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 36 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 40:

AAACAACCTT TACTTCGTAG AAGTAAATTG GTTAAG

36

30 (2) INFORMATION FOR SEQ ID NO: 41:

35 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 32 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

40

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 41:

TGAGAGGTTA GTACTTCTCA GTATGTTTGT TC

32

(2) INFORMATION FOR SEQ ID NO: 42:

50 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

55 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

5 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 42:

10 AGGCAC TATG CTTGAAGCAT CGC

23

(2) INFORMATION FOR SEQ ID NO: 43:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 38 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 43:

GTTAGCATAA ATAGGTAAC T ATTATGACA CAAGTAAC

38

30

(2) INFORMATION FOR SEQ ID NO: 44:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 36 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

40

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 44:

45

AGTTAGCATA AGTAGTGTAA CTATTTATGA CACAAG

36

(2) INFORMATION FOR SEQ ID NO: 45:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

55 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 45:

10 GGAAGAAGCC TGAGAAAGTT TCTGAC

26

(2) INFORMATION FOR SEQ ID NO: 46:

15 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 33 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

20 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 46:

GCATTTATAT GTAAGAGCAA GCATTCTATT TCA

33

(2) INFORMATION FOR SEQ ID NO: 47:

30 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 22 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

35 (iii) HYPOTHETICAL: NO

40 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 47:

45 GAGTAGCGTG GTGAGGACGA GA

22

(2) INFORMATION FOR SEQ ID NO: 48:

50 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

55 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 48:

GGATAACTGT CTTAGGACGG TTTGAC

26

10 (2) INFORMATION FOR SEQ ID NO: 49:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 30 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

20 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 49:

ATCGGTGGTA AATTAAACCC AAATCCCTGT

30

(2) INFORMATION FOR SEQ ID NO: 50:

30 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 30 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

35 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 50:

CAGTTCTGAA AGAACATTT CGCTTCTTTC

30

45 (2) INFORMATION FOR SEQ ID NO: 51:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 30 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

55

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 51:

CACCCATTAA TTTTTTCGGT GTTAAAACCC

30

10

(2) INFORMATION FOR SEQ ID NO: 52:

15

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

20

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 52:

CAAAACTGAA AACGACAATC TTTCTAGTTC C

31

30

(2) INFORMATION FOR SEQ ID NO: 53:

35

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 30 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

40

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 53:

TACCAAGCAA AACCGAGTGAA ATAAAGAGTT

30

50

(2) INFORMATION FOR SEQ ID NO: 54:

55

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 54:

CAGAAGATGC GGAATAACGT GAC

23

(2) INFORMATION FOR SEQ ID NO: 55:

10 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 26 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

15 (ii) MOLECULE TYPE: cDNA
 (iii) HYPOTHETICAL: NO

20 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 55:

25 AACGAAGCCG TATGTGAGCA TTTGAC

26

(2) INFORMATION FOR SEQ ID NO: 56:

30 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 31 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

35 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 56:

GAACGTAACT TCATGTTAAC GTTGACTTA T

31

(2) INFORMATION FOR SEQ ID NO: 57:

45 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 27 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

55 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 57:

GCTTAAGTGC ACAGTGCTCT AAACTGA

27

(2) INFORMATION FOR SEQ ID NO: 58:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 27 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 58:

CACGGTAATT AGTGTGATCT GACGAAG

27

(2) INFORMATION FOR SEQ ID NO: 59:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 22 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 59:

CGTGCCGCCT TCGTTTCTCT TT

22

(2) INFORMATION FOR SEQ ID NO: 60:

45 (i) SEQUENCE CHARACTERISTICS:

- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

— 1 —

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 60:

5 TTCGCTTCGG GGTGGATCTG TG

22

(2) INFORMATION FOR SEQ ID NO: 61:

(i) SEQUENCE CHARACTERISTICS:

10 (A) LENGTH: 28 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

15 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 61:

CAAAACTGAC TTACGAGTCA CGTTTGAG

28

25 (2) INFORMATION FOR SEQ ID NO: 62:

(i) SEQUENCE CHARACTERISTICS:

30 (A) LENGTH: 25 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

35 (iii) ANTI-SENSE: NO

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 62:

GATGTATGCT TCGTTATTCC ACGCC

25

(2) INFORMATION FOR SEQ ID NO: 63:

45 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

50 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

55

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 63:

5 GGTCAAAACCT CCAGGGACGC C

21

(2) INFORMATION FOR SEQ ID NO: 64:

10 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

15 (ii) MOLECULE TYPE: cDNA

20 (iii) HYPOTHETICAL: NO

25 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 64:

30 GCGGTAATGT GTGAAAGCGT TGCC

24

(2) INFORMATION FOR SEQ ID NO: 65:

35 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

40 (iii) HYPOTHETICAL: NO

45 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 65:

50 TCCCTTGTTGG CCTGTGTG

18

(2) INFORMATION FOR SEQ ID NO: 66:

55 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 19 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

55 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 66:

TCCTTCATCG GCTCTTCGA

19

5 (2) INFORMATION FOR SEQ ID NO: 67:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 18 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

10 (ii) MOLECULE TYPE: cDNA

15 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 67:

GATGCCAAGG CATCCACC

18

25 (2) INFORMATION FOR SEQ ID NO: 68:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 19 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 68:

CCTCCCACGT CCTTCATCG

19

40 (2) INFORMATION FOR SEQ ID NO: 69:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 22 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

50 (iii) ANTI-SENSE: NO

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 69:

AAGGTTTCTG ACTAGGTTGG GC

22

(2) INFORMATION FOR SEQ ID NO: 70:

5

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 22 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

10

(ii) MOLECULE TYPE: cDNA

15 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 70:

20

GGTGAAGTGC TTGCATGGAT CT

22

(2) INFORMATION FOR SEQ ID NO: 71:

25

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 23 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

30

(ii) MOLECULE TYPE: cDNA

35

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 71:

ACCTGTGAGT TTTCGTTCTT CTC

23

40

(2) INFORMATION FOR SEQ ID NO: 72:

45

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 24 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

50

(ii) MOLECULE TYPE: cDNA

55

(iii) HYPOTHETICAL: NO

50

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 72:

55

CTATTTGTTC AGTTTGAGA GGTT

24

(2) INFORMATION FOR SEQ ID NO: 73:

5 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

10 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 73:

20 ATTTTCCGTA TCAGCGATGA TAC

23

(2) INFORMATION FOR SEQ ID NO: 74:

25 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

30 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 74:

ACGAAGTAAA GGTTGTTTT CT

22

(2) INFORMATION FOR SEQ ID NO: 75:

40 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 25 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

50 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 75:

55 GAGAGGTTAC TCTCTTTAT GTCAG

25

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(2) INFORMATION FOR SEQ ID NO: 76:

5 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 275 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

10 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 76:

20 AAGGAGCACC ACGAAAACGC CCCAACTGGT GGGGCGTAGG CCGTGAGGGG TTCTTGTCTG 60
TAGTGGGCGA GAGCCGGGTG CATGACAACA AAGTTGGCCA CCAACACACT GTTGGGTCCCT 120
GAGGCAACAC TCGGACTTGT TCCAGGTGTT GTCCCACCGC CTTGGTGGTG GGGTGTGGTG 180
TTTGAGAACT GGATAGTGGT TCGGAGCATC AATGGATAACG CTGCCGGCTA GCGGTGGCGT 240
25 GTTCTTTGTG CAATATTCTT TGGTTTTGT TGTGT 275

(2) INFORMATION FOR SEQ ID NO: 77:

30 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 278 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

35 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 77:

45 AAGGAGCACC ACGAAAAGCA CCCAACTGG TGGGGTGCAG GCCGTGAGGG GTTCCCGTCT 60
GTAGTGGACG GGGGCCGGNT GCGCAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT 120
GAGACAACAC TCGGTCCGTC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT 180
TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAGCGCA TGGTCTTCGT GGCCGGCGTT 240
50 CATCGAAATG TGTAATTCT TCCTTAACTC TTGTGTGT 278

(2) INFORMATION FOR SEQ ID NO: 78:

55 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 278 base pairs
(B) TYPE: nucleic acid

(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

5 (iii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 78:

AAGGAGCACC ACGAAAAGCA CCCCAACTGG TGGGGTGCAGA GCCGTGAGGG GTTCCCGTCT	60
GTAGTGGACG GGGGCCGGGT GCACAAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT	120
GAGACAACAC TCGGTCCGTC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT	180
TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAGCGCA TGGTCTTCGT GGCCGGCGTT	240
CATCGAAATG TGTAATTCT TTTTAACTC TTGTGTGT	278

(2) INFORMATION FOR SEQ ID NO: 79:

25 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 280 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 79:

AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCAGA GCCGTGAGGG GTTCCCGTCT	60
GTAGTGGACG GGGGCCGGNT GCACAAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT	120
GAGACAACAC TCGGTGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT	180
TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAGCGCA TAGTCTTGT GGCTGATGCG	240
CTCGTCGAAA TGTGTAATTCTT CTTCTTGTT GTNTGTGTGT	280

(2) INFORMATION FOR SEQ ID NO: 80:

50 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 281 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

55 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 80:

10	AAGGAGCACC ACGAAAAGCA TCCCAATTGG TGGGGTGCAGA GCCGTGAGGG GTTCTCGTCT	60
	GTAGTGGACG AAAACCGGGT GCACAAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT	120
	GAGACAACAC TCGGTCGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT	180
15	TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAGCGCG TAGTCCTTG TGGCTGATGC	240
	GTTCATCAAATGTGTAATT TCTTTTTGG TTTNTGTGTG T	281

(2) INFORMATION FOR SEQ ID NO: 81:

20 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 280 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 81:

35	AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCAGA GCCGTGAGGG GTTCCCGTCT	60
	GTAGTGGACG GGGGCCGGGT GCACAAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT	120
	GAGACAACAC TCGGTCGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT	180
40	TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAGCGCA TAGCCCTTGC GGCTGATGCG	240
	TTCGNCGAAA TGTGTAATT CTTCTCTGGT TTCTGTGTGT	280

(2) INFORMATION FOR SEQ ID NO: 82:

45 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 282 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

50 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 82:

5	AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCAGA GCCGTGAGGG GTTCTCGTCT	60
	GTAGTGGACG GNAGCCGGGT GCACAAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT	120
	GAGACAAACAC TCGGTCGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT	180
10	TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAGCGCG TAGTCCTTCG TGGCTGATGC	240
	GTTCATCGAA ATGTGTAATT TCTTCTTTGG TTTTGGGTGT GT	282

(2) INFORMATION FOR SEQ ID NO: 83:

15	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 282 base pairs
	(B) TYPE: nucleic acid
	(C) STRANDEDNESS: single
	(D) TOPOLOGY: linear
20	(ii) MOLECULE TYPE: cDNA
	(iii) HYPOTHETICAL: NO
25	(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 83:

30	AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCAGA GCCGTGAGGG GTTCCCCTCT	60
	GTAGTGGACG GGGGCCGGGT GCACAAACAGC AAATGATCGC CAGACACACT ATTGGGCCCT	120
	GAGACAAACAC TCGGTCGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT	180
35	TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAGCGCA TAGTCCTTTG GGGCTGATGT	240
	GTTTCATCAA AATGTGTAAT TTCTTTTNG GTTTTNGTGT GT	282

(2) INFORMATION FOR SEQ ID NO: 84:

40	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 281 base pairs
	(B) TYPE: nucleic acid
	(C) STRANDEDNESS: single
	(D) TOPOLOGY: linear
45	(ii) MOLECULE TYPE: cDNA
	(iii) HYPOTHETICAL: NO
50	(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 84:

55	AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCAGA GCCGTGAGGG GTTCTCGTCT	60
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5 GTAGTGGACG GGAGCCGGT GCACAAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT 120
 GAGACAAACAC TCGGTGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT 180
 TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAGCCGC TAGTCCTTCG TGGCTGATGC 240
 GTTCAATTGAA ATGTGTAATT TCTTCTCTGG TTTTTGTGTG T 281

10 (2) INFORMATION FOR SEQ ID NO: 85:

15 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 280 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: cDNA

25 (iii) HYPOTHETICAL: NO

30 (iv) ANTI-SENSE: NO

35 (xii) SEQUENCE DESCRIPTION: SEQ ID NO: 85:

40 AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCAGA GCCGTGAGGG GTTCCCGTCT 60
 GTAGTGGACG GGGGCCGGGT GCACAAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT 120
 GAGACAAACAC TCGGTGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT 180
 TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAGCCGA TAGTCCTTGT GGCTGATGCG 240
 CTCGTCGAAA TGTGTAATTG CTTCTTTGGT TTTTGTGTGT 280

45 (2) INFORMATION FOR SEQ ID NO: 86:

50 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 282 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

55 (ii) MOLECULE TYPE: cDNA

60 (iii) HYPOTHETICAL: NO

65 (iv) ANTI-SENSE: NO

70 (xiii) SEQUENCE DESCRIPTION: SEQ ID NO: 86:

75 AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCAGA GCCGTGAGGG GTTCCCGTCT 60
 GTAGTGGACG GGGGCCGGGT GCGCAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT 120
 GAGACAAACAC TCGGTGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTTGGTGT 180
 TTGAGTATTG GATAAGTGGTT GCGAGCATCT AGATGAGCCGC GTAGTCCTTG TGGCTGATGC 240

GTTCGTCGAA ATGTGTAATT TCTTCTTTGG GTTTTGTGT GT

282

5 (2) INFORMATION FOR SEQ ID NO: 87:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 281 base pairs
 (B) TYPE: nucleic acid
 10 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

15 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

20 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 87:

AAGGAGCACC ACGAAAAGCA CCCCAATTGG TGGGGTGCAG CCGTGAGGG GTTCTCGTCT	60
GTAGTGGACG GNAGCCGGNT GCGAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT	120
25 GAGACAACAC TCGGNCGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTNGTGT	180
TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGGCGCG TAGTCCTTG TGACTGATGC	240
GTTCATCAA ATGTGTAATT TCTTCTTTGN NTTTNGTGTG T	281

30 (2) INFORMATION FOR SEQ ID NO: 88:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 281 base pairs
 (B) TYPE: nucleic acid
 35 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

40 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 88:

AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCAG CCGTGAGGG GTTCTCGTCT	60
GTAGTGGACG GGAACCGGGT GCACAAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT	120
50 GAGACAACAC TCGGTCGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT	180
TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAGCGCA TAGTCCTTG TGGCTGACGC	240
GTTCATCGAA ATGTGTAATT TCTTCTTTGG TTTTNGTGTG T	281

55 (2) INFORMATION FOR SEQ ID NO: 89:

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(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 280 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 89:

AAGGAGCACC	ACGAAAAGCA	CTCCAAATTGG	TGGGGTGCAG	GCCGTGANGG	GTTCGGTCT	60
GTAGTGGACG	GGGGCCGGGT	GCACAAACAGC	AAATGATTGC	CAGACACACT	ATTGGGCCCT	120
GAGACAAACAC	TCGGTCGATC	CGTGTGGAGT	CCCTCCATCT	TGGTGGTGGG	GTGTGGTGT	180
TGAGTATTGG	ATAGTGGTTG	CGAGCATCTA	GATGAGCGCA	TAGTCCTTAG	GGCTGATGCG	240
TTCGTCGNAA	TGTGTAATTT	CTTCTTTGGT	TTTTGTGTG			280

(2) INFORMATION FOR SEQ ID NO: 90:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 282 base pair
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 90:

AAGGAGCACC	ACGAAAAGCA	TCCCAATTGG	TGGGGTGCAG	GCCGTAGGG	GTTCTCGTCT	60
CTAGTGGACG	AAAACCGGGT	GCACAAACAGC	AAATAATTGC	CAGACACACT	ATTGGGCCCT	120
GAGACAAACAC	TCGGTCGATC	CGTGTGGTGT	CCCTCCATCT	TGGTGGTGGG	GTGTGGTGT	180
TGAGTATTGG	ATAGTGGTTG	CGAGCATCTA	GATGAACGCG	TAGTCCTTCG	TGGCTGACGT	240
GTTCATCGAA	ATGTGTAATT	TCTTNTNTTA	ACTCTTGTTG	GT		282

(2) INFORMATION FOR SEQ ID NO: 91:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 280 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 91:

AAGGAGCACC ACGAAAAGCA CCCCAATTGG TGGGTGCGA GCCGTGAGGG GTTCTCGTCT	60
GTAGTGGACG GGAGCCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT	120
GAGACAACAC TCGGTCAGTC CGTGTGGTGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT	180
TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAACGCG TAGTCCTTGT GACTGACGTG	240
TTCATCGAAA TGTGTAATTT CTTTCTAAC TCTTGTGTGT	280

20 (2) INFORMATION FOR SEQ ID NO: 92:

25 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 281 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 92:

AAGGAGCACC ACGAAAAGCA CTTCAATTGG TGAAGTGCAGA GCCGTGAGGG GTTCTCGTCT	60
GTAGTGGACG AAAGCCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT	120
GAGACAACAC TCGGTCGAAC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT	180
TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAACGCG TGGTCTTCAT GGCCGGCGTG	240
TTCATCGAAA TGTGTAATAT CTTCTCTGGT TTTCGGTGTG T	281

40 (2) INFORMATION FOR SEQ ID NO: 93:

45 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 280 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

50 (ii) MOLECULE TYPE: cDNA

55 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 93:

AAGGAGCACC ACGAAAAGCA CTTCAATTGG TGAAGTGCAGA GCGGTGAGGG GTTCTCGTCT	60
10 GTAGTGGACG AAAACCGGNT GCACAAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT	120
GAGACAACAC TCGGTCGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT	180
TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAACGCG TGGTCTTCAT GGCCGGCGTG	240
15 TTCATCGAAA TGTGTAATTT CTTTTNNAC TCTTGTGTGT	280

(2) INFORMATION FOR SEQ ID NO: 94:

20 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 280 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 94:

AAGGAGCACC ACGAAAAGCA CTTCAATTGG TGAAGTGCAGA GCGGTGAGGG GTTCTCGTCT	60
35 GTAGTGGACG AAAGCCGGT GCACAAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT	120
GAGACAACAC TCGGTCGAAC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT	180
TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAACGCG TGGTCTTCAT GGCCGGCGTG	240
40 TTCATCGAAA TGTGTAATTT CTTCTTGTT TTTNGTGTGT	280

(2) INFORMATION FOR SEQ ID NO: 95:

45 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 281 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

50 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 95:

	AAGGAGCACC ACGAAAAGCA CTTCAATTGG TGAAGTGCAGA GCCGTGAGGG GTTCTCGTCT	60
5	GTAGTGGACG AAAACCGGGT GCACAAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT	120
	GAGACAACAC TCGGTCGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT	180
	TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAACCGG TAGTCCTTCG NGGNNCNGCGT	240
10	GTTCATCGAA ATGTGTAATT TCTNTNTAA CTCTNGTGTG T	281

(2) INFORMATION FOR SEQ ID NO: 96:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 281 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 96:

	AAGGAGCACC ACGAAAAGCA TCCAATTGG TGGGGTGTGA GCCGTGAGGG GTTCTCGTCT	60
30	GTAGTGGACG AAAACCGGGT GCACAAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT	120
	GAGACAACAC TCGGTCGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT	180
	TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAACCGG TAGTCCTTCG GGGCCGGCGT	240
35	GTTCATCGAA ATGTGTAATT TCTTTTTAA CTCTTGTGTG T	281

(2) INFORMATION FOR SEQ ID NO: 97:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 280 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 97:

	AAGGAGCACC ACGAAAAGCA CTTCAATTGG TGAAGTGCAGA GCCGTGAGGG GTTCTCGTCT	60
55	GTAGTGGACG AAAACCGGGT GCACAAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT	120

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5 GAGACAAACAC TCGGTGGAAC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT 180
TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAACGCG TGGTCTTCAT GGCCGGCGTG 240
TTCATCGAAA TGTGTAATT TCTTCTTAAC TCTTGTGTGT 280

(2) INFORMATION FOR SEQ ID NO: 98:

10 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 280 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

15 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 98:

25 AAGGAGCACC ACGAAAAGCA CTTCAATTGG TGAAGTGCAGA GCCGTGAGGG GTTCTCGTCT 60
GTAGTGGACG AAAACCGGGT GCACAAACAGN AAATGATTGC CAGACACACT ATTGGGCCCT 120
GAGACAAACAC TCGGTGCGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT 180
30 TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAACGCG TGGTCTTCAT GGCCNGCGTG 240
TTCATCGAAA TGTGTAATT TCTTCTTAAC TCTTGTGTGT 280

(2) INFORMATION FOR SEQ ID NO: 99:

35 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 280 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 99:

50 AAGGAGCACC ACGAAAAGCA CTTCAATTGG TGAAGTGCAGA GCCGTGAGGG GTTCTCGTCT 60
GTAGTGGACG AAAACCGGGT GCACAAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT 120
GAGACAAACAC TCGGTGCGATC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT 180
55 TGAGTATTGG ATAGTGGTTG CGAGCATCTA GATGAACGCG TGGTCTTCAT GGCCGGCGTG 240
TTCATCGAAA TGTGTAATT TCTTCTTAAC TCTTGTGTGT 280

(2) INFORMATION FOR SEQ ID NO: 100:

5 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 281 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 10 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

15 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 100:

20	AAGGAGCACC ACGAAAAGCA CCCCAACTGG TGGGGTGCAGA GCCGTGAGGG GTCCTCGCCT	60
	GTAGTGGCG GGGGCCGGGT GCACAAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT	120
25	GAGGCAACAC TCGGCTCGTT CTGAGTGGTG TCCCTCCATC TTGGTGGTGG GGTGTGGTGT	180
	TTGAGTATTG GATA GTGGTT GCGAGCATCT AACCGGATGC GTGCCGGCA ACGGTGGCGT	240
	GTTCGTTGAA ATGTGTAATT TCTTTTTGG TTTTTGTGTG T	281

(2) INFORMATION FOR SEQ ID NO: 101:

30 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 274 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 35 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

40 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 101:

45	AAGGAGCACC ACGAAAAGCA TCCCAACAAG TGGGGTGCAGA NCCGTGAGGG GTTCTCGTCT	60
	GTAGTGGACG AAAGCCGGGT GCACGACAAC AAGCAAAGCC AGACACACTA TTGGGTCCCTG	120
50	AGGCAACACT CGGGCTCTGT TCGAGAGTTG TCCCACCATC TTGGTGGTGG GGTGTGGTGT	180
	TTGAGAATTG GATA GTGGTT GCGAGCATCA AATGGATGCG TTGCCCTACG GGTAGCGTGT	240
	TCTTTGTGC AATTTTATTC TTTGGTTTT GTGT	274

(2) INFORMATION FOR SEQ ID NO: 102:

55 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 293 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 102:

AAGGAGCACC ATTTCCCAGT CGATGAAC TA GGGAACATAA AGTAGGCATC TGTAGTGGAT	60
ATCTACTTGG TGAATATGTT TTGTAAATCC TGTCCACCCCC GTGGATGGGT AGTCGGCAAA	120
ACGTCGGACT GTCATAAGAA TTGAAACGCT GGCACACTGT TGGGTCCCTGA GGCAACACGT	180
TGTGTTGTCA CCCTGCTTGG TGGTGGGGTG TGGACTTITGA CTTCTGAATA GTGGTTGCGA	240
GCATCTAAAC ATAGCCTCGC TCGTTTTCTGA GTGGGGCTGG TTTTGCATT TTA	293

(2) INFORMATION FOR SEQ ID NO: 103:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 296 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 103:

AAGGAGCACC ATTTCCCAGT CGGATGAAC TGGAAACATA AAGTAGGCAT CTGTAGTG	60
TATCTACTTG GTGAATATGT TTTGTAAATC CTGTCACCC CCGTGGATGG TAGTCGGCA	120
AAACGTCGGA CTGTCATAAG AATTGAAACG CTGGCACACT GTGGGTCCT GAGGCAACAC	180
GTTGTGTTGT CACCCCTGCTT GGTGGTGGGG TGTGGACTTT GACTTCTGAA TAGTGGTTGC	240
GAGCATCTAA ACATAGCCTC GCTCGTTTC GAGTGAGGCT GTTTTTGCA ATTTTA	296

(2) INFORMATION FOR SEQ ID NO: 104:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 274 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 104:

AAGGAGCACC	ACGAAGAGCA	CTCCAATTGG	TGGGGTGC _{GA}	GCCGTGAGGG	GTCATCGTCT	60
GTAGTGGACG	AAGACCGGGT	GCACGACAAC	AAGCTAAGCC	AGACACACTA	TTGGGTCC _{TG}	120
15 AGGCAACACC	CTCGGGTGCT	GTCCCCCAT	CTTGGTGGTG	GGGTGTGGTG	TTTGAGAATT	180
GGATAGTGGT	TGCGAGC _{ATC}	AAAATGTATG	CGTTGTC _{GTT}	CTCGGCAACG	TGTTCTTTT	240
GTGCAATT _{TA}	TTCTTTGGTT	TTTGTAGTGT	TTGT			274

20 (2) INFORMATION FOR SEQ ID NO: 105:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 278 base pairs
 (B) TYPE: nucleic acid
 25 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

30 (iii) ANTI-SENSE: NO

35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 105:

AAGGAGCACC	ACGAAGAGCA	CTCCAATTGG	TGGGGTGC _{GA}	GCCGN _G AGGG	GTCATCGTCT	60
GTAGTGGACG	AAGACTGGGT	GCACGACAAC	AAAGCAAGCC	AGACACACTA	TTGGGTCC _{TG}	120
40 AGGCAACACC	CTCGGGTGCT	GCCCC _T CCAT	CTTGGTGGTG	GGGTGTGGTG	TTTGAGAACT	180
GGATAGTGGT	TGCGAGC _{ATC}	AAAATGTAT	GC _G TGTC _G _T	TCGCGACAAC	GTGTTCTTT	240
TGTGCAATT _{TA}	ATTCTTTT	GGTTTTGGTA	GTGTTTGT			278

45 (2) INFORMATION FOR SEQ ID NO: 106:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 276 base pairs
 (B) TYPE: nucleic acid
 50 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

55 (iii) ANTI-SENSE: NO

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 106:

	AAGGAGCACC ACGAGAAGCA CTCCAATTGG TGGGGTGCAA GCCGTGAGGG GTCATCGTCT	60
10	GTAGTGGACG AAGACCGGGT GCACGACAAC AAGCAAAGCC AGACACACTA TTGGGTCTG	120
	AGGCAACACC CTCGGGTGCT GTCCCCCAT CTTGGTGGTG GGGTGTGGTG TTTGAGAACT	180
	GGATAAGTGGT TGCGAGCATC AAAATGTATG CGTTGTCGTT CGCGGCAACG TGGTCTTTT	240
15	GTGCAATTTC TATTCTTGG TTTTGTAGT GTTTGT	276

(2) INFORMATION FOR SEQ ID NO: 107:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 277 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- 25 (iii) HYPOTHETICAL: NO
- (iii) ANTI-SENSE: NO

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 107:

	AAGGAGCACC ACGAAAAGCA CCCCAATTGG TGGGGTGCAA GCCGTGAGGG GTTCCCGCCT	60
35	GTAGTGGGCC GGGCCGGGTG CGCAACACAGCA AATGATTGCC AGACACACTA TTGGGCCCTG	120
	AGGCAACACT CGGATCGATT GAGTGCTTGT CCCCCCATCT TGGTGGTGGG GTGTGGTGT	180
	TGAGAACTGG ATAGTGGTTG CGAGCATCTA AATGAACGCA CTGCCGATGG TGGTGTGTT	240
40	GTTTGTGTA ATTATTATTCT TTGGTTTTTG TGTTTGT	277

(2) INFORMATION FOR SEQ ID NO: 108:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 282 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: cDNA
- 45 (iii) HYPOTHETICAL: NO
- (iii) ANTI-SENSE: NO

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 108:

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AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGC_G GA GCCGTNAGGG GTTCTCGTCT 60
5 GTAGTGGATG GCAGCCGGT GCACANCAGC AAATGATTGC CAGACACACT ATTGGGCCCT 120
GAGACAAACAC TCGGTCAGTC CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGNGTT 180
TGAGTATTGG ATAGTGGTTG CGANCATCTA GATGAACCGG TAGTCCTCNG TGGCTGACGT 240
10 GTTCATCAAA ATGTGTAATT TCTTTTANGG GTTTNGGTGT CT 282

(2) INFORMATION FOR SEQ ID NO: 109:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 280 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

20 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 109:

AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGC_G GA GCCGNAGGG GTTCTCGCCT 60
30 GTAGTGNCG AGGGCCGGAT GCACAACAAAC ACATGATTGC CAGACACACT ATTGGGCCCT 120
GANACAAACAC TCGGCCAGTC CGTGTGGTGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT 180
TGAGTATNGG ATAGTNGTG NGANCATCTA AACGGCTGCG TNGNCNNGAA CGGTGGCGTG 240
35 TTCGNTAAAA TGTGTAATT TCTTTNNNGGT TTGGGTGTNT 280

(2) INFORMATION FOR SEQ ID NO: 110:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 280 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

45 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 110:

AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGC_G GA GCCGTGAGGG GTTCTCGCCT 60
55 GTAGTGGCG ANGGCCGGT GCACAACAAAC AAATGATTGC CAGACACACT ATTGGGCCCT 120
GAGACAAACAC TCGGCCAGTC CGTGTGGTGT CCCNCCATCT TGGTGGTGGG GTGTGGTGT 180

TGAGTATTGG ATAGTGGTTG CGAGCATCTA AANGNTGCG TTGCCNNAN CNGTGGCGTN 240
 5 TTCGNTAAAA TGTGTAANTT CTTTTTNGGT TTGTGTGTGT 280

(2) INFORMATION FOR SEQ ID NO: 111:

10 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 471 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

15 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 111:

ATCGAAGATC CCGGCTTCTT CATAAGCTCC CACACGAATT GCTTGATTCA CTGGTTAGAC 60
 25 GATTGGGTCT GTAGCTCAGT TGGTTAGAGC GCACCCCTGA TAAGGGTGAG GTCGGCAGTT 120
 CGAACATCTGCC CAGACCCACC AATTGTTGGT GTGCTGCCTG ATCCGATAACG GGGCCATAGC 180
 TCAGCTGGGA GAGCGCCTGC TTTGCACGCA GGAGGTCAGG AGTCGATCC TCCTTGGCTC 240
 30 CACCATCTAA AACAAATCGTC GAAAGCTCAG AAATGAATGT TCGTGGATGA ACATTGATTT 300
 CTGGTCTTTG CACCAGAACT GTTCTTTAAA AATTGGGTA TGTGATAGAA GTAAGACTGA 360
 ATGATCTCTT TCACTGGTGA TCATTCAAGT CAAGGTAAGA TTTGCGAGTT CAAGCGCGAA 420
 35 TTTTCGGCGA ATGTCGTCTT CACAGTATAA CCAGATTGCT TGGGGTTATA T 471

(2) INFORMATION FOR SEQ ID NO: 112:

40 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 520 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 112:

ATCGAAGACA TCAGCTTCTT CATAAGTATC CACACGAATT GCTTGATTCA TAGTCGAACG 60
 55 AATGCTGTAA CGCGACCCGT GTTATAGGTC TGTAGCTCAG TTGGTTAGAG CGCACCCCTG 120

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5 ATAAGGGTGA GGTCGGCAGT TCAAATCTGC CCAGACCTAC CAATTGCTTG GTCGAGAAGA 180
ATACGGGGCC ATAGCTCAGC TGGGAGAGCG CCTGCCTTGC ACGCAGGAGG TCAGCGGTTC 240
GATCCCGCTT GGCTCCACCA CTCTCTCGTG TTGCGGTGAG TGTTAAAGAG TTCAGAAATG 300
ATGCCGCTTC AGGTTTGTCC TGTTGAGTGC TGATTCTGG TCTTTGACC GGTACGAAAA 360
10 TCGTTCTTAA AAAATTGGA TATGTGATAG AAGTGACTGA TTAATTGCTT TCACTGGCAA 420
TTGATCTGGT CAAGGTAAA TTTGTAGTTC TCAAGACGCA AATTTTCGGC GAATGTCGTC 480
TTCACGATTG AGACAGTAAC CAGATTGCTT GGGGTTATAT 520

15 (2) INFORMATION FOR SEQ ID NO: 113:

20 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 504 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: cDNA

30 (iii) HYPOTHETICAL: NO

35 (iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 113:

40 ATCGAAGACA CCGGCTTCGT CATAAGCTCC CACACGAATT GCTTGATTCA CTTGCAGAAAG 60
GCGATTGGGT TTAGACCCGA GAGTAACGAT TGGGTCTGTA GCTCAGTTGG TTAGAGCGCA 120
CCCCTGATAA GGGTGAGGTC GGCAGTCGA ATCTGCCAG ACCCACCAAT CGAAGGGGCC 180
45 ATAGCTCAGC TGGGAGAGCG CCTGCTTGC ACGCAGGAGG TCAGCGGTTC GATCCCGCTT 240
GGCTCCACCA TAAACTCTAG TCGCCGAAAG CTCAGAAATG AGTGTCTTACG AGGATGAGGT 300
TGATTGCTG GTTGAACAT TGATTCTGG ACTTTGCGCC AGAACTGTTTC TTTAAAAATT 360
TGGGTATGTG ATAGAAGTAG ACCGATGTGT TGCTTCACT GGCAGCATGT CGCGTCAAGG 420
TAAAATTTGC GTGTTCTCTA TGCAAATTTT CGGCGAATGT CGTCTTCACG TTATAGACAG 480
TAACCAGATT GCTTGGGGTT ATAT 504

(2) INFORMATION FOR SEQ ID NO: 114:

50 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 499 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

55 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 114:

10	ATCGAAGACT TCAGCTTCTT CATAAGTTCC CACACGAATT GCTTGATTCA CTTGCAGAAA	60
	GCGATTGGGT TGAGACCCGA GAGTGACGAT TGGGTCTGTA GCTCAGTTGG TTAGAGCGCA	120
	CCCCTGATAA GGGTGAGGTC GGCAGTTCGA ATCTGCCAG ACCCACCAAT TGTCGGGATG	180
15	GCCAGTGTCA AATGGGGCCA TAGCTCAGCT GGGAGAGCGC CTGCTTGCA CGCAGGAGGT	240
	CAGGAGTTCG ATCCTCCTTG GCTCCACCCT CAACTCACGA TCGCTGAAAG CTCAGAAATG	300
	AACATTGGTA GTTCAATGTT GATTTCTGGT CTTTGCGCCA GAACTGTTCT TTAAAAAATT	360
20	GGGTATGTGA TAGAAAGTGAC TAACAGCGTG TTTCACTGCA CGTTGTTAAT CAAGGCAGAA	420
	TTTGCAGTT CAAGCGCGAA TTTTCGGCGA ATGTCGTCTT CACGTTACGA ATCTATAACC	480
	AGATTGCTTC GGGTTATAT	499

25 (2) INFORMATION FOR SEQ ID NO: 115:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 468 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: cDNA

35 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 115:

40	ATCGACGACA TCAGCTGTCT CATAAGCTCC CACACGAATT GCTTGATTCA TTGAAGAAGA	60
	CGATTAGGTT AGCAACCTTC GATTGGGTCT GTAGCTCAGT TGGTTAGAGC GCACCCCTGA	120
45	TAAGGGTGAG GTCGGCAGTT CGAACATGCC CAGACCCACC AATTGCTGG GGCCATAGCT	180
	CAGCTGGGAG AGCGCCTGCC TTGCACGCAG GAGGTCAGCG GTTCGATCCC GCTTGGCTCC	240
	ACCACCCCGC TTGCCAGTT GTCAAAGCTT AGAAATGAAT ATTCCGCTCG AATATTGATT	300
50	TCTGAACTTT ATCAGAACATCG TTCTTTAAAA ATTTGGGTAT GTGATAGAAA GATAGACTGG	360
	ACAGCACTTT CACTGGTGTG TGTCAGGCT AAGGTAAAAT TTGTGAGTAA TTACAAGTTT	420
	TCGGCGAATG TTGTCTTCAC AGTATAACCA GATTGCTTGG GGTTATAT	468

55 (2) INFORMATION FOR SEQ ID NO: 116:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 246 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 116:

TAAGGAAAAAG GAAACCTGTG AGTTTTCGTT CTTCTCTGTT TGTCAGTTT TGAGAGGTTA 60
ATTCTTCTCT ATACTGTTTG TTCTTTGAAA ACTAGATAAG AAAGTTAGTA AAGTTAGCAT 120
AAATAGGTAA CTATTTATGA CACAAGTAAC CGAGAACAT CTGAAAGTGA ATCTTTCATC 180
TGATTGGAAG TATCATCGCT GATACGAAAAA ATCAGAAAAAA CAACCTTTAC TTCATCGAAG 240
TAAATT 246

(2) INFORMATION FOR SEQ ID NO: 117:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 246 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 117:

CTAAGGAAAA GGAAACCTGT GAGTTTCGT TCTTCTCTAT TTGTTCAAGTT TTGAGAGGTT 60
AGTACTTCTC AGTATGTTTG TTCTTGAAA ACTAGATAAG AAAGTTAGTA AAGTTAGCAT 120
AGATAATTAA TTATTTATGA CACAAGTAAC CGAGAAATCAT CTGAAAGTGA ATCTTTCATC 180
TGATTGGAAAG TATCATCGCT GATACGGAAA ATCAGAAAAAA CAACCTTTAC TTCGTAGAAG 240
TAAATT 246

(2) INFORMATION FOR SEQ ID NO: 118:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 246 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

5 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 118:

TAAGGAAAAG GAAACCTGTG AGTTTCGTT CTTCTCTGTT TGTTCAGTTTGAGAGGTTA	60
TTACTTCTCT GTATGTTGT TCTTGAAAAA CTAGATAAGA AAGTTAGTAA AGTTAGCATA	120
ACTAGTGTAAC CTATTTATGA CACAAGTAAC CGAGAACATCTGAAAGTGA ATCTTTCATC	180
TAATTCGACG TATCATCGCT GATACAGACA ATTAGAAAAAA CAACCTTTAC TTGACCGAAG	240
TAAATT	246

20 (2) INFORMATION FOR SEQ ID NO: 119:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 363 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 119:

GGCCTATAGC TCAGCTGGTT AGAGCGCACG CCTGATAAGC GTGAGGTCGA TGGTTCGAGT	60
CCATTTAGGC CCACCTTTTC TTTCTGACAG AAGAAACACT GTATAACCTA TTTAAGGGGC	120
CTTAGCTCAG CTGGGAGAGC GCCTGCTTGCACGAGAG GTCAGCGGTT CGATCCCGCT	180
AGGCTCCACC AAAATTGTTT TTTGAAAAGTAAAGATAAGAAA GTTAGTAAAG TTAGCATAAA	240
TAGGTAACCA TTTATGACAC AAGTAACCGA GAATCATCTG AAAGTGAATC TTTCATCTGA	300
TTGGAAGTAT CATCGCTGAT ACGAAAAATC AGAAAAACAA CCTTTACTTC ATCGAAGTAA	360
ATT	363

50 (2) INFORMATION FOR SEQ ID NO: 120:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 496 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 120:

TAAGGAAAAG	GAAACCTGTG	AGTTTCGTT	CTTCTCTATT	TGTCAGTTT	TGAGAGGTTA	60
CTCTCTTTA	TGTCAGATAA	AGTATGCAAG	GCACATGCT	TGAAGCATCG	CGCCACTACA	120
15 TTTTGACGG	GCCTATAGCT	CAGCTGGTTA	GAGCGCACGC	CTGATAAGCG	TGAGGTCGAT	180
GGTCGAGTC	CATTTAGGCC	CACTTTTCT	TTCTGACATA	AGAAATACAA	ATAATCATAAC	240
20 CCTTTTACGG	GGCCTTAGCT	CAGCTGGGAG	AGCGCCTGCT	TTGCACGCAG	GAGGTCAGCG	300
GTTCGATCCC	GCTAGGCTCC	ACCAAAATTG	TTCTTTGAAA	ACTAGATAAG	AAAGTTAGTA	360
AAGTTAGCAT	AGATAATTAA	TTATTTATGA	CACAAGTAAC	CGAGAACAT	CTGAAAGTGA	420
25 ATCTTTCATC	TGATTGGAAG	TATCATCGCT	GATAACGGAA	ATCAGAAAAA	CAACCTTTAC	480
TTCGTAGAAG	TAAATT					496

(2) INFORMATION FOR SEQ ID NO: 121:

30 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 498 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

35 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 121:

TAAGGAAAAG	GAAACCTGTN	AGTTTNCGTN	CTTCTCTGTT	TGTCAGTTT	TNAGAGGTTA	60
45 CTCTCTTTNA	TGTCAGATAA	AGTACGCACG	GCACGTTGCC	TTGGGCAAAG	AGCCACTACA	120
TTATTGACGG	GCCTATAGCT	CAGCTGGTTA	GAGCGCACGC	CTGATAAGCG	TGAGGTCGAT	180
GGTCGAGTC	CATTTAGGCC	CACTTTTCT	TTCTGACAGA	AGAAATCATT	TGCACATCCT	240
50 ATTAATAAGG	GNCCCTAGCT	CAGCTGGGAG	AGCGCCTGCT	TTGCACGCAG	GAGGTCAGCG	300
GTTCGATCCC	GCTAGGCTCC	ACCCAAAATT	GTTCTTGAA	AACTAGATAA	AAAAGTTAGT	360
55 AAAGTTAGCA	TAAGTACTAT	AACTATTTAT	GACACAAGTA	ACCGAGAACATC	ATCTGAAAGT	420
GAATCTTTCA	TCTAATTGCA	CGTATCATCG	CTGATACAGA	CAATTNGAAA	ACAAACCTT	480

ACTTCGACGA AGTAAATT

498

5 (2) INFORMATION FOR SEQ ID NO: 122:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 229 base pairs
 (B) TYPE: nucleic acid
 10 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 122:

TAAGGATAAG GATAACTGTC TTAGGACGGT TTGACTAGGT TGGGCAAGCG TTTTTTTAAT	60
CTTGTATTCT ATTCCTTTTG CATTGTTAACG CGTTGTTCC AAAACATTAA GTTTACGATC	120
AAGTATGTTA TGTAATAAT ATGGTAACAA GTAAATTACAC ATATAATAAT AGACGTTAA	180
GAATATATGT CTTTAGGTGA TGTTAACTTG CATGGATCAA TAATTACAA	229

25 (2) INFORMATION FOR SEQ ID NO: 123:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 248 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 123:

TAAGGATAAG GAAGAAGCCT GAGAAGGTTT CTGACTAGGT TGGGCAAGCA TTTATATGTA	60
AGAGCAAGCA TTCTATTTCA TTTGTGTTGT TAAGAGTAGC GTGGTGAGGA CGAGACATAT	120
AGTTTGTGAT CAAGTATGTT ATTGTAAAGA AATAATCATG GTAACAAGTA TATTCACGC	180
ATAATAATAG ACGTTTAAGA GTATTTGTCT TTTAGGTGAA GTGCTTGCAT GGATCTATAG	240
AAATTACAA	248

35 (2) INFORMATION FOR SEQ ID NO: 124:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 224 base pairs

(B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

10 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 124:

15 CAAATGGAGT TTTTATTTT TATTTATCTT AAACACCCAT TAATTTTTTC GGTGTTAAAA	60
CCC AAATCAA TGTTGGTCT CACAACTAAC ACATTTGGTC AGTTGTATC CAGTTCTGAA	120
AGAATGTTT TGAACAGTTC TTTCAAAACT GAAAACGACA ATCTTCTAG TTCCAAAAT	180
20 AAATACCAAA GGATCAATAC AATAAGTTAC TAAGGGCTTA TGGT	224

(2) INFORMATION FOR SEQ ID NO: 125:

25 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 252 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 125:

40 CTAATGAAGT TTTTTACTTT TTCTTTTCAT CTATAATAAA GATAAATACT AAACAAAACA	60
TCAAAATCCA TTTATTTATC GGTGGTAAAT TAAACCCAAA TCCCTGTTG GTCTCACAAAC	120
TAACATATTG GGTCAGATTG TATCCAGTTC TGAAAGAACAA TTTCCGCTTC TTTCAAAACT	180
45 GAAAACGACA ATCTTCTAG TTCCAAATAA ATACCAAAGG ATCAATACAA TAAGTTACTA	240
AGGGCTTATG GT	252

(2) INFORMATION FOR SEQ ID NO: 126:

50 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 608 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

55 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 126:

10	AACGAAAGAT TGACGATTGG TAAGAATCCA CAACAAGTTG TTCTTCATAG ATGTATCTGA	60
	GGGTCTGTAG CTCAGTTGGT TAGAGCACAC GCTTGATAAG CGTGGGGTCA CAAGTTCAAG	120
	TCTTGTCAAG CCCACCAGA CTTTGACTGG TTGAAGTTAT AGATAAAAGA TACATGATTG	180
15	ATGATGTAAG CTGGGGACTT AGCTTAGTTG GTAGAGCGCC TGCTTGCAC GCAGGAGGTC	240
	AGGAGTCGA CTCTCCTAGT CTCCACCAGA ACTTAAAGATA AGTCGGATT ACAGAAATTA	300
	GTAAATAAAG ATTGAGATCT TGGTTTATTA ACTTCTGTGA TTTCATTATC ACGGTAATT	360
20	GTGTGATCTG ACGAAGACAC ATTAACATCA TAACAGATTG GCAAAATTGA GTCTGAAATA	420
	AATTGTCAC TCAAGAGTTT AGGTTAACAGCA ATTAATCTAG ATGAATTGAG AACTAGCAA	480
	TTAACTGAAT CAAGCGTTTT GGTATGTGAA TTTAGATTGA AGCTGTACAG TGCTTAAGTG	540
25	CACAGTGCTC TAAACTGAAA TGTTGAAGTT ACTAACTTGT AGGTAACATC GACTGTTGG	600
	GGTTGTAT	608

(2) INFORMATION FOR SEQ ID NO: 127:

30

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 269 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

35

- (ii) MOLECULE TYPE: cDNA

40

- (iii) HYPOTHETICAL: NO

- (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 127:

45	AACGAAAGAT TGACGATTGG TAAGAATCCA CGACAAGTTG TTCTTCATAG ATGTATCTGA	60
	GGGTCTGTAG CTCAGTTGGT TAGAGCACAC GCTTGATAAG CGTGGGGTCA CAAGTTCAAG	120
	TCTTGTCAAG CCCACCAGA CTTTGACTGG TTGAAGTTAT AGAAAAGAAG ATACATAACT	180
50	GATGATGTAAG GCTGGGGACT TAGCTTAGTT GGTAGAGCGC CTGCTTGCAC CGCAGGAGGT	240
	CAGGAGTTCG ACTCTCCTAG TCTCCACCA	269

(2) INFORMATION FOR SEQ ID NO: 128:

55

- (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 249 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 128:

AACGAAAGAT TGATGGCCGG TAAGAATCCA CAACAAGTTG TTCTTCGAAG ATGTATCTGA 60
GGGTCTGTAG CTCAGTTGGT TAGAGCACAC GCTTGATAAG CGTGGGGTCA CAAGTTCAAG 120
TCTTGTCAAG CCCACCAAAT CTGAAAGATA TGTGTTCAT TATGATTAAA GCTGGGGACT 180
TAGCTTAGTT GGTAGAGCGC CTGCTTGCA CGCAGGAGGT CAGGAGTTCG ACTCTCCTAG 240
TCTCCACCA 249

(2) INFORMATION FOR SEQ ID NO: 129:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 283 base pair
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 129:

AACGAAAGAT	TGACGATTGG	TAAGAATCCA	CAACAAGTTG	TTCTTCATGA	CGATGTATCT	60
GAGGGTCTGT	AGCTCAGTTG	GTTAGAGCAC	ACGCTTGATA	AGCGTGGGGT	CACAAGTTCA	120
AGTCTTGTCA	GACCCACCAA	ATCTGACTAA	CAAGCATTAT	TAAATGCTGA	ATACAGAAAA	180
ACAGAGACAT	TGACTTATTG	ATAAGCTGGG	GACTTAGCTT	AGTTGGTAGA	GCGCCTGCTT	240
TGCACGCAGG	AGGTCAAGGAG	TTCGACTCTC	CTAGTCTCCA	CCA		283

(2) INFORMATION FOR SEQ ID NO: 130:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 283 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

5 (iii) ANTI-SENSE: NO

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 130:

AACGAAAGAT	TGGTGACCGG	TAAGAATCCA	CAACAAGTTG	TTCTTCGAAG	ATGTATCTGA	60
GGGTCTGTAG	CTCAGTTGGT	TAGAGCACAC	GCTTGATAAG	CGTGGGTCA	CAAGTTCAAG	120
15 TCTTGTCAAG	CCCACCACTA	CTGACGAAGT	GATGAATAAT	CACAAGCTGC	TAGATGAAAA	180
GATATGTCGT	TCATTATGAT	TAAAGCTGGG	GACTTAGCTT	AGTTGGTAGA	GCGCCTGCTT	240
TGCACGCAGG	AGGTCAGGAG	TTCGACTCTC	CTAGTCTCCA	CCA		283

20 (2) INFORMATION FOR SEQ ID NO: 131:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 808 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

30 (iii) ANTI-SENSE: NO

35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 131:

TAAGGAAGAT	CGAGAATTGG	AAAGAGGTG	GATTTATCCG	GATGATCCTT	CTCCATCTTA	60
TTAGAACATA	GATCGCAGGC	CAGTCAGCCT	GACGATCGCT	TGCAGGCGTG	CCGCCTTCGT	120
40 TTCTCTTTCT	TCATTGTTGA	TTGCTCACGG	GCCGTACCGC	AGCTGACGCT	GCTGGCCCTG	180
CGCAGGCGCG	GCCCCATCAGG	GCCGACGGCC	GGTCGGCCTT	GCNAAGCTTC	GCTTCGGGGT	240
GGATCTGTGG	ATCGCGTAGT	AGCGTTGGC	TCGGTATCTG	GGCTTGTAGC	TCAGTIGGTT	300
45 AGAGCACACG	CTTGATAAGC	GTGGGGTCGG	AGGTTCAAGT	CCTCCCAGGC	CCACCAAAGTT	360
ACTTGATGAG	GGGCCGTAGC	TCAGCTGGGA	GAGCACCTGC	TTTGCAAGCA	GGGGGTCGTC	420
50 GGTCGATCC	CGTCCGGCTC	CACCATCATG	TTGGTGTGTA	GACGGATATT	GGCAATCAAC	480
AAAAGAAAGA	AACAAGTTG	CGGACTNTTA	CGAAAGTCTG	CCTGTTCTGT	ATGAAATCGT	540
GAAGAGAAGA	TGTAATCGGA	TCAACTGAAG	AGTTGATGTC	GCAAGAAGCT	TGCTCAAGCC	600
TTGCATAATG	ATTGATGTGT	TTAACCGCCA	TCACCGATTG	TATCTCGAGA	AGCTGGTCTT	660
55 TCTGCTGATA	CTGTTGAAAC	GAGCATTGTC	AGTCGAATGG	CAACATTCTGG	CGTCGCATAAA	720

TGGGGCTTTA AGAGCTGAGT TTTGATGGAT ATTGGCAATG AGAGTGATCA AGTGTCTTAA 780

5 GGGCATTGGT GGATGCCTTG GCATGCAC 808

(2) INFORMATION FOR SEQ ID NO: 132:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 808 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

10 15 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 132:

TAAGGAGGAT CGAGAACATTGG AAAGAGGCCG GATTTATCCG GATGATCCTT CTCCATCTTA 60

25 TTAGAACATA GATCGCAGNC CAGTCAGCCT GACGATCGCT TGCAGGCCGT CGGCCTTCGT 120

TTCTCTTTCT TCATTGTTGA TTGCTCACGG GCCGTACCGC AGCTGACGCT GCTGGCCCTG 180

CGCAGGCCG GNCCATCAGG GCCGACGGCC GGTCGGCCTT GCGAAGCTTC GCTTCGGGGT 240

30 GGATCTGTGG ATCGCGTAGT AGCGTTGCG TCGGTATCTG GGCTTGTAGC TCAGTTGGTT 300

AGAGCACACG CTTGATAAGC GTGGGGTCGG AGGTTCAAGT CCTCCCAGGC CCACCAAGTT 360

ACTTGATGAG GGGCCGTAGC TCAGCTGGGA GAGCACCTGC TTTGCAAGCA GGGGGTCGTC 420

35 GGTCGATCC CGTCCGGCTC CACCATCATG TTGGTGTGAA GACGGATATT GGCAATCAAC 480

AAAAGAAAGA AACAAAGTTTG CGGACTNTTA CGAAAGTCTG CCTGTTCTGT ATGAAATCGT 540

GAAGAGAAGA TGTAATCGGA TCAACTGAAG AGTTGATGTC GCAAGAAGCT TGCTCAAGCC 600

40 TTGCATAATG ATTGATGTGT TTAACCGCCA TCACCGATTG TATCTCGAGA AGCTGGTCTT 660

TCTGCTGATA CTGTTGAAAC GAGCATTGAG AGTCGAATGG CAACATTCGG CGTCGCATAA 720

45 TGCGGCTTTA AGAGCTGAGT TTTGATGGAT ATTGGCAATG AGAGTGATCA AGTGTCTTAA 780

GGGCATTGGT GGATGCCTTG GCATGCAC 808

(2) INFORMATION FOR SEQ ID NO: 133:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 353 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

55 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 133:

10	CCTTAAAGAA CTGTTCTTG CAGTGCTCAC ACAGATTGTC TGATGAAAAG TAAATAGCAA	60
	GGCGTCTTGC GAAGCAGACT GATACTCCC CTTCGTCTAG AGGCCAGGA CACCGCCCTT	120
	TCACGGCGGT AACAGGGGTT CGAATCCCCT AGGGGACGCC ACTTGCGCGG TAATGTGTGA	180
15	AAGCGTTGCC ATCAAGTATCT CAAAAGTAC TTACGAGTCA CGTTTGAGAT ATTTGCTCTT	240
	TAAAAAATCTG GATCAAGCTG AAAATTGAAA CACAGAACAA CGAAAGTTGT TCGTGAGTCT	300
	CTCAAATTTT CGCAACACGA TGATGAATCG TAAGAAAACAT CTTCGGGTTG TGA	353

20 (2) INFORMATION FOR SEQ ID NO: 134:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 515 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

30 (iii) ANTI-SENSE: NO

35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 134:

	CCTTAAAGAA CTGTTCTTG CAGTGCTCAC ACAGATTGTC TGATGAAAAA CGAGCAGTAA	60
	AACCTCTACA GGCTTGTAGC TCAGGTGGTT AGAGCGCACC CCTGATAAGG GTGAGGTCGG	120
40	TGGTTCAAGT CCACTCAGGC CTACCAAATT TTCCCTGAAT ACTGCGTTGT GAAATAACTC	180
	ACATACTGAT GTATGCTTCG TTATTCCACG CCTTGTCTCA GGAAAAATTAA TCGGTAAAGA	240
	GGTTCTGACT ACACGATGGG GCTATAGCTC AGCTGGGAGA GCGCCTGCTT TGCACGCAGG	300
45	AGGTCTGCGG TTCACTCCCCG CATAGCTCCA CCATATCGTG AGTGTTCACG AAAAAAATCT	360
	TCAGAGTCTTA CCTGAAAGGG TTCACTGCGA AGTTTGCTC TTTAAAAATC TGGATCAAGC	420
	TGAAAAATTGA AACACAGAAC AACGAAAGTT GTTCGTGAGT CTCTCAAATT TTCGCAACAC	480
50	GATGATGAAT CGTAAGAAC ATCTCGGGT TGTGA	515

(2) INFORMATION FOR SEQ ID NO: 135:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 353 base pairs
- (B) TYPE: nucleic acid

(C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 135:

15	CCTTAAAGAA GCGTACTTTG CAGTGCTCAC ACAGATTGTC TGATGAAAAG TAAATAGCAA	60
	GGCGTCTTGC GAAGCAGACT GATACTCCC CTTCGTCTAG AGGCCAGGA CACCGCCCTT	120
	TCACGGCGGT AACAGGGGTT CGAATCCCCT AGGGGACGCC ACTTGCGCGG TAATGTGTGA	180
20	AAGCGTTGCC ATCAGTATCT CAAAACGTAC TTACGAGTCA CGTTTGAGAT ATTTGCTCTT	240
	TAAAAAATCTG GATCAAGCTG AAAATTGAAA CACAGAACAA CGAAAGTTGT TCGTGAGTCT	300
	CTCAAATTTT CGAACACAGA TGATGAATCG TAAGAAACAT CTTCGGGTTG TGA	353

25 (2) INFORMATION FOR SEQ ID NO: 136:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 481 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

35 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 136:

40	CCTTAAAGAA CTGTTCTTG AAGTGCTCAC ACAGATTGTC TGATGAAAAA CGAGCAGTAA	60
	AACCTCTACA GGCTTGTAGC TCAGGTGGTT AGAGCGCACC CCTGATAAGG GTGAGGTCGG	120
	TGGTTCAAGT CCACTCAGGC CTACCAAATT TTCCCTGAAT ACTGCGTTGT GAAATAACTC	180
45	ACATACTGAT GTATGCTTCG TTATTCCACG CCTTGTCTCA GGAAAAATTAA TCGGTAAAGA	240
	GGTTCTGACT ACACGATGGG GCTATAGCTC AGCTGGGAGA GCGCCTGCTT TGACACGAGG	300
50	AGGTCTGCGG TTGATCCCCG CATAGCTCCA CCATCTCGTG AGTGTTCACG AAAAAAATCT	360
	TCAGAGTGTAA CCTGAAAGGG TTCACTGCGA AGTTTGCTC TTTAAAAATC TGGATCAAGC	420
	TGAAAATTGA AACACAGAAC AACGAAAGTT GTTCGTGAGT CTCTCAAATT TTGCAACAC	480
55	G	481

(2) INFORMATION FOR SEQ ID NO: 137:

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 392 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

10 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 137:

CCTTAAAGAA GCGTACTTTG AAGTGCTCAC ACAGATTGTC TGATGAAAAG TGAATAGCAA	60
20 GGCGTCTTGC GATTGAGACT TCAGTGTCCC CTTCGTCTAG AGGCCAGGA CACCGCCCTT	120
TCACGGCGGT AACAGGGGTT CGAACATCCCCT AGGGGACGCC AGCGTTCAAA CTGATGAGGT	180
CAAACCTCCA GGGACGCCAC TTGCTGGTTT GTGAGTGAAA GTCACCTGCC TTAATATCTC	240
25 AAAACTGACT TACGAGTCAC GTTTGAGATA TTTGCTCTTT AAAAATCTGG ATCAAGCTGA	300
AAATTGAAAC ACAGAACAAAC GAAAGTTGTT CGTGAGTCTC TCAAATTTTC GCAACACGAT	360
GATGAATCGT AAGAAACATC TTCGGGTTGT GA	392

30

(2) INFORMATION FOR SEQ ID NO: 138:

(i) SEQUENCE CHARACTERISTICS:

35 (A) LENGTH: 515 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

40

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 138:

CCTTAAAGAA ACGGTCTTTG AAGTGCTCAC ACAGATTGTC TGATGAAAAA CGAGCAGTAA	60
AACCTCTACA GGCTTGTAGC TCAGGGTGGTT AGAGCGCACC CCTGATAAGG GTGAGGTCGG	120
50 TGGTTCAAGT CCACTCAGGC CTACCAAATT TTCCCTGAAT ACTGCGTTGT GAAATAACTC	180
ACATACTGAT GTATGCTTCG TTATTCCACG CCTTGTCTCA GGAAAAATTG TCGGTAAAGA	240
GGTTCTGACT ACACGATGGG GCTATAGCTC AGCTGGGAGA GCGCCTGCTT TGCACGCAGG	300
55 AGGTCTGCAGG TTGATCCCCG CATAGCTCCA CCATCTCGTG AGTGTAAACG AAAAAATACT	360

TCAGAGTGTA CCTGAAAGGG TTCACTGCGA AGTTTGCTC TTTAAAAATC TGGATCAAGC 420
 5 TGAAAATTGA AACACAGAAC AACGAAAGTT GTTCGTGAGT CTCTCAAATT TTGCGAACAC 480
 GATGATGAAT CGTAAGAAC ATCTTCGGGT TGTGA 515

(2) INFORMATION FOR SEQ ID NO: 139:

10 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 365 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

15 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

20 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 139:

25 CTAAGGATAT ATTCCGAACA TCTTCTTCGG AAGATGCGGA ATAACGTGAC ATATTGTATT 60
 CAGTTTGAA TGTTTATTAA ACATTCAAAT ATTTTTGGT TAAAGTGATA TTGCTTTGA 120
 AAATAAGCA GTATGCGAGC GCTTGACTAA AAAAAATTGT ACATTGAAAA CTAGATAAGT 180
 30 AAGTAAAATA TAGATTTAC CAAGCAAAAC CGAGTGAATA AAGAGTTTA AATAAGCTTG 240
 ATTTCATAAG AAATAATCGC TAGTGTTCGA AAGAACACTC ACAAGATTAA TAACGCGTTT 300
 AAATCTTTTT ATAAAAGAAC GTAACTTCAT GTAACGTTT GACTTATAAA AATGGTGGAA 360
 35 ACATA 365

(2) INFORMATION FOR SEQ ID NO: 140:

40 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 548 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 140:

CTAAGGATAT ATTCCGAACA TCTTCTTCAG AAGATGCGGA ATAACGTGAC ATATTGTATT 60
 55 CAGTTTGAA TGTTTATTAA ACATTCAAAT ATTTTTGGT TAAAGTGATA TTGCTTATGC 120

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	GAGCNCTTGA CAATCTATTG TTTTAAAGA AAGCGGTTGT CAGACAATGC ATTAAGAAAA	180
5	ATTAAGCGG AGTTTACTTT TGAAATGAG CATTGATTT TTTGAAAATA AAGCAGTATG	240
	CGAGCGCTTG ACTAAAAGA AATTGTACAT TGAAAAC TAG ATAAGTAAGT AAAATATAGA	300
	TTTACCAAG CAAAACCGAG TGAATAAAAGA GTTTAAATA AGCTTGAATT CATAAGAAAT	360
10	AATCGCTAGT GTTCGAAAGA ACACTCACAA GATTAATAAC GCGTTAAAT CTTTTATCAA	420
	AAGAAAACGT TTAGCAGACA ATGAGTTAAA TTATTTAAA GCAGAGTTA CTTATGTAAA	480
	TGAGCATTAA AAATAATGAA AACGAAGCCG TATGTGAGCA TTTGACTTAT AAAATGGTG	540
15	GAAACATA	548

(2) INFORMATION FOR SEQ ID NO: 141:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 471 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 141:

	CTAAGGATAT ATT CGGAACA TCTTCTTCAG AAGATGCGGA ATAACGTGAC ATATTGTATT	60
35	CAGTTTGAA TGT TTATTTA ACATTCAAAT ATTTTTGGT TAAAGTGATA TTGCTTATGC	120
	GAGCGCTTGA CAATCTATTG TTTTAAAGA AAGCGGTTGT CAGACAATGC ATTAAGAAAA	180
	ATTAAGCGG AGTTTACTTT TGAAATGAG CATTGATTT TTTGAAAATA AAGCAGTATG	240
40	CGAGCGCTTG ACTAAAANGA AATTGTACAT TGAAAAC TAG ATAAGTAAGT AAAATATAGA	300
	TTTACCAAG CAAAACCGAG TGAATAAAAGA GTTTGAATA AGCTTGAATT CATAAGAAAT	360
	AATCGCTAGT GTTCGAAAGA ACACTCACAA GATTAATAAC GCGTTAAAT CTTTTATCAA	420
45	AAGAACGTAA CTTCATGTTA ACGTTGACT TATAAAAATG GTGGAAACAT A	471

(2) INFORMATION FOR SEQ ID NO: 142:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 383 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 142:

10	CTAAGGATAT ATT CGGAACA TCTT CTTCA G AAG ATGC GGA ATA AC GTGAC AT ATT GTATT	60
	CAG NTTTGAA TGTTTATTTA ACATTC AAAA AATGGGCCTA TAGCTCAGCT GGTTAGAGCG	120
	CAC GCCTGAT AAG CGT GAGG TCGGTGGTTC GAGTCCACTT AGGCCACCA TTATTTGTAC	180
15	ATTGAAA ACT AGATAAGTAA GTAAAATATA GATTTTACCA AGCAAAACCG AGTGAATAAA	240
	GAGTTTAAA TAAGCTGAA TTCATAAGAA ATAATCGCTA GTGTTCGAAA GAACACTCAC	300
	AAGATTAATA ACGCGTTAA ATCTTTTAT AAAAGAACGT AAC TCATGT TAACGTTGA	360
20	CTTATAAAAA TGGTGGAAAC ATA	383

(2) INFORMATION FOR SEQ ID NO: 143:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 351 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

30

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 143:

40	CTAAGGATAT ATT CGGAACA TCTT CYTCAG AAG ATGC GGA ATA ATGTGAC AT ATT GTATT	60
	CAGTTTGAA TGTTTATTTA ACATTC AAAT ATTTTTGGT TAAAGTGATA TTGCTTATGC	120
	GAG GCCTTGA CTAAAAGAA ATTGTACATT GAAA ACTAGA TAAGTAAGTA AAANTATAGA	180
	TTTTACCAAG CAAA ACCGAG TGAATAAGA GTTTAAATA AGCTTGAATT CATAAGAAAT	240
45	AATCGCTAGT GTTCGAAAGA ACACTCACAA GATTAATAAC GCGTTAAAT CTTTTATCAA	300
	AAGAACGTAA CTTCATGTTA ACGTTGACT TATAAAAATG GTGGAAACAT A	351

(2) INFORMATION FOR SEQ ID NO: 144:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 263 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

55

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 144:

10	CTAAGGATAT ATTGGAAACA TCTTCTACGA AGATGAGGGA ATAACGTGAC ATATTGTATT	60
	CAGTTTGAA TGTTTATTAA CATTCAATTG TACATTGAAA ACTAGATAAG TAAGTAAGAT	120
	TTTACCAAGC AAAACCGAGT GAATAGAGTT TAAATAAGC TTGAATTCAT AAATAATCGC	180
15	TAGTGTTCGA AAGACNTCCA CAAGATTAAT AACTAGTTT AGCTATTTAT TTTGAATAAC	240
	AATTCAAAAT ATGGTGGGAC ATA	263

(2) INFORMATION FOR SEQ ID NO: 145:

20	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 247 base pairs
	(B) TYPE: nucleic acid
	(C) STRANDEDNESS: single
	(D) TOPOLOGY: linear

25	(ii) MOLECULE TYPE: cDNA
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(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 145:

35	AAGGATAAGG AACTGCACAT TGGTCTTGTT TAGTCTTGAG AGGTCTTGTG GGGCCTTAGC	60
	TCAGCTGGGA GAGCGCCTGC TTTGCACGCA GGAGGTCAGC GGTCGATCC CGCTAGGCTC	120
	CATTGGTGAG AGATCACCAA GTAATGCACA TTGAAAATTG AATATCTATA TCAAATAGTA	180
40	ACAAGAAAAT AAACCGAAAA CGCTGTAGTA TTAATAAAGA GTTATGACT GAAAGGTCAA	240
	AAAATAA	247

(2) INFORMATION FOR SEQ ID NO: 146:

45	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 375 base pairs
	(B) TYPE: nucleic acid
	(C) STRANDEDNESS: single
	(D) TOPOLOGY: linear

50	(ii) MOLECULE TYPE: cDNA
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(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

55

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 146:

5 AAGGAAATGG AACACGTTTA TCGTCTTATT TAGTTTGAG AGGTCTTGTG GGGCCTTAGC 60
TCAGCTGGGA GAGCGCCTGC TTNGCACGCA GGAGGTCAGC GGTCGATCC CGCTAGGCTC 120
CATCAGGATA CANTCCTACT AAACCTAATA CAACTGAAGT TGAACACGCA ACTCACTTCC 180
10 TAGGAAAATA GACAATCTTC GCTTGTGTGC AAGGCACACA TGGTCAGATT CCTAATTTTC 240
TACAGAAGTT TCGCTAAAGC GAGCGTTGCT TAGTATCCTA TATAATAGTC CATNGAAAAT 300
TGAATATCTA TATCAAATTC CACGATCTAG AAATAGATTG TGGAAACGTA ACAAGAAATT 360
15 AACCCGNAAA CGCTG 375

(2) INFORMATION FOR SEQ ID NO: 147:

20 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 244 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: cDNA

 (iii) HYPOTHETICAL: NO

 (iv) ANTI-SENSE: NO

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 147:
AAGGATAAGG AACTGCACAT TGGTCTTGTGTT TAGTCTTGAG AGGTCTTGTG GGGCCTTAGC 60

35 TCAGCTGGGA GAGCGCCTGC TTTGCACGCA GGAGGTCAGC GGTCGATCC CGCTAGGCTC 120
CATTGGTGAG AGATCACCAA GTAATGCACA TTGAAAATTG AATATCTATA TCAAATAGTA 180
ACAAGAAAAT AAACCGAAAC GCTGTAGTAT TAAAAGAGTT TATGACTGAA AGGTCAGAAA 240
40 ATAA 244

(2) INFORMATION FOR SEQ ID NO: 148:

45 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 284 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

50 (ii) MOLECULE TYPE: cDNA

 (iii) HYPOTHETICAL: NO

 (iv) ANTI-SENSE: NO

55

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 148:

5 CTAAGGATAT ATTGGAAACA TCTTCTTACG AAGATGCAGG AATAACATTG ACATATTGTA 60
TTCAGNTGTG AATGCTCATT GGAGNATTCA TNGCATNATT TGGTNCATTG ACANCTAGAT 120
AAGNAAGTAA AATTTATGAT TTTACCAAGC AAAACCGAGT GAATTAGAGT TNTNNAACAA 180
10 GCTTGATTT CAAAAAGAAA TAATCGCTAG TGTTGAAAG AACACTCACA GATTANTAAC 240
ATCTTGGGTTT TTCACCCGAC TTGTTCGTNT CGAAAGTCAA AAAA 284

(2) INFORMATION FOR SEQ ID NO: 149:

15 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 246 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 149:

30 AAGGATAAGG AACTGCGCAT TGGTCTTGT TAGTCTTGAG AGGTCTTGTG GGGCCTTAGC 60
TCAGCTGGGA GAGCGCCTGC TTTGCACGCA GGAGGTCAGC GGTCGATCC CGCTAGGCTC 120
CATTGGTGAG AGATCACCAA GTAATGCACA TTGAAAATTG AATATCTATA TCAAATAGTA 180
35 ACAAGAAAAT AAACCGAAAA CGCTGTAGTA TTAATAAGAG TTTATGACTG AAAGGTCAA 240
AAATAA 246

(2) INFORMATION FOR SEQ ID NO: 150:

40 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 247 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 150:

55 AAGGATAAGG AACTGCGCAT TGGTCTTGT TAGTCTTGAG AGGTCTTGTG GGGCCTTAGC 60
TCAGCTGGGA GAGCGCCTGC TTTGCACGCA GGAGGTCAGC GGTCGATCC CGCTAGGCTC 120

CATTGGTGAG AGATCACCAA GTAATGCACA TTGAAAATTG AATATCTATA TCAAATAGTA 180
 5 ACAAGAAAAT AAACCGAAAA CGCTGTAGTA TTAATAAGAG TTTATGACTG AAAGGTCAGA 240
 AAAATAA 247

(2) INFORMATION FOR SEQ ID NO: 151:

10 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 247 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

15 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

20 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 151:

25 AAGGAAAAGG AACTGCGCAT TGGTCTTGTGTT TAGTCTTGAG AGGTCTTGTG GGGCCTTAGC 60
 TCAGCTGGGA GAGCGCCTGC TTTGCACGCA GGAGGTCAGC GGTCGATCC CGCTAGGCTC 120
 CATTGGTGAG AGATCACCAA GTAATGCACA TTGAAAATTG AATATCTATA TCAAATAGTA 180
 30 ACAAGAAAAT AAACCGAAAA CGCTGTAGTA TTAATAAGAG TTTATGACTG AAAGGTCAGA 240
 AAAATAA 247

(2) INFORMATION FOR SEQ ID NO: 152:

35 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 244 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

45 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 152:

50 AAGGATAAGG AACTGCGCAT TGGTCTTGTGTT TAGTCTTGAG AGGTCTTGTG GGGCCTTAGC 60
 TCAGCTGGGA GAGCGCCTGC TTTGCACGCA GGAGGTCAGC GGTCGATCC CGCTAGGCTC 120
 CATTGGTGAG AGATCACCAA GTAATGCACA TTGAAAATTG AATATCTATA TCAAATAGTA 180
 55 ACAAGAAAAT AAACCGAAAC GCTGTAGTAT TAAAAGAGTT TATGACTGAA AGTCAGAAA 240

ATAA

244

(2) INFORMATION FOR SEQ ID NO: 153:

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 153:

20	AAGGATAAGG AACTGCGCAT TGGTCTTGTT TAGTCTTGAG AGGTCTTGTG GGGCCTTAGC	60
	TCAGCTGGGA GAGCGCCTGC TTTGCACGCA GGAGGTCAGC GGTCGATCC CGCTAGGCTC	120
	CATTGGTGAG AGATCACCAA GTAATGCACA TTGAAAATTG AATATCTATA TCAAATAGTA	180
25	ACAAGAAAAT AAACCGAAAC GCTGTAGTAT TAAAAGAGTT TATGACTGAA AGGTCAAAAA	240
	TAA	243

(2) INFORMATION FOR SEQ ID NO: 154:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 809 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 154:

45	TAAGGAAGAT CGAGAACATTGG AAAGAGGTCG GATTATCCG GATGATCCTT CTCCATCTTA	60
	TTAGAACATA GATCGCAGGC CAGTCAGCCT GACGATCGCT TGCAGGCGTG CCGCCCTCGT	120
	TTCTCTTCT TCATTGTTGA TTGCTCACGG GCCGTACCGC AGCTGACGCT GCTGGCCCTG	180
50	CGCAGGCGCG GCCCATCAGG GCCGAACGGC CGGTCGGCCT TGCNAAGCTT CGCTTCGGGG	240
	TGGATCTGTG GATCGCGTAG TAGCGTTGC GTGGGTATCT GGGCTTGAG CTCAGTTGGT	300
	TAGAGCACAC GCTTGATAAG CGTGGGGTCG GAGGTTCAAG TCCTCCCAGG CCCACCAAGT	360
55	TACTTGATGA GGGGCCGTAG CTCAGCTGGG AGAGCACCTG CTTTGCAAGC AGGGGGTCGT	420

CGGTCGATC CCGTCCGGCT CCACCATCAT GTTGGTGTG AGACGGATAT TGGCAATCAA 480
 5 CAAAAGAAAG AAACAAGTTT GCGGACTNTT ACGAAAGTCT GCCTGTTCTG TATGAAATCG 540
 TGAAGAGAAG ATGTAATCGG ATCAACTGAA GAGTTGATGT CGCAAGAACG TTGCTCAAGC 600
 CTTGCATAAT GATTGATGTG TTTAACCGCC ATCACCGATT GTATCTCGAG AAGCTGGTCT 660
 10 TTCTGCTGAT ACTGTTGAAA CGAGCATTG CAGTCGAATG GCAACATTG GCGTCGCATA 720
 ATGCCGCTTT AAGAGCTGAG TTTTGATGGA TATTGGCAAT GAGAGTGATC AAGTGTCTTA 780
 AGGGCATTGG TGGATGCCTT GGCAATGCAC 809

15 (2) INFORMATION FOR SEQ ID NO: 155:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 23 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: cDNA

25 (iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 155:

TGGGGTGAAG TCGTAACAAAG GTA

23

(2) INFORMATION FOR SEQ ID NO: 156:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 21 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 156:

CCTTTCCCTC ACGGTACTGG T

21

50 (2) INFORMATION FOR SEQ ID NO: 157:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 277 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 157:

AAGGAGCACC ACGAGAAACA CTCCAATTGG TGGGGTGTAA GCGGTGAGGG GTTCTCGTCT	60
GTAGTGGACG GAAGCCGGGT GCACAACAAAC AAGCAAGCCA GACACACTAT TGGGTCCCTGA	120
GGCAACATCT CTGTTGGTTT CGGGATGTTG TCCCACCATC TTGGTGGTGG GGTGTGGTGT	180
TTGAGAATTG GATA GTGGTTT GCGAGCATCA ATTGGATGCG CTGCCTTTTG GTGGCGTGTT	240
CTGTTGTGCA ATTTTATTCT TTGGTTTTTG TGTTTAT	277

(2) INFORMATION FOR SEQ ID NO: 158:

25 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 286 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

30

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 158:

AAGGAGCACC ACGAGAAACA CCCCAATTGG TGGGGTGTGA GCGGTGAGGG GTTCTCGTCT	60
GTAGTGGACG AGGGCCGGGT GCACAACAAAC AGGCAATCGC CGGACACACT ATTGGGCCCT	120
GAGACAACAC TCGGCCGACT GAGGTCGACG TGGTGTCCCT CCATCTTGGT GGTGGGGTGT	180
GGTGTGGAG CATTGAATAG TGGTTGCGAG CATCTAGCCG GATGCGTTCC CCAGTGGTGC	240
GCCTTCGTCA AAAATGTGTA ATTTTCTTT TGTTTTTGT GTTCGT	286

(2) INFORMATION FOR SEQ ID NO: 159:

50 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 286 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

55

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 159:

10	AAGGAGCACC ACGAGAAACA CCCCAATTGG TGGGGTGTGA GCCGTGAGGG GTTCTCGTCT	60
	GTAGTGGACG AGGGCCGGGT GCACAACAAAC AGGCAATCGC CGGACACACT ATTGGGCCCT	120
	GAGACAACAC TCGGCCGACT GAGGTCGACG TGGTGTCCCT CCATCTTGGT GGTGGGGTGT	180
15	GGTGTGAG CATTGAATAG TGGTTGCGAG CATCTAGACG GATGCGTTCC CCAGTGGTGC	240
	GCGTTCGTCA AAAATGTGTA ATTTTCTTT TGGTTTTGT GTTCGT	286

(2) INFORMATION FOR SEQ ID NO: 160:

20

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 279 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

25

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 160:

35	AAGGAGCACC ACGAGAAACA CCCCAATTGG TGGGGTGTGA GCCGTGAGGG GTTCTCGTCT	60
	GTAGTGGACG AGGCAGGTAC AACAAACGCCA ATCGCCGGAC ACACATTGG GCCTGAGACA	120
	ACACTCGGCC GACTGAGGTC GACGTGGTGT CCCTCCATCT TGGTGGTGG GTGTGGTGT	180
40	TGAGCATTGA ATAGTGGTTG CGAGCATCTA GCCGGATGCG TTCCCCAGTG GTGCCGCTTC	240
	GTCAAAAATG TGTAATTTT CTTTGGTTT TGTGTTCGT	279

(2) INFORMATION FOR SEQ ID NO: 161:

45

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 288 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

50

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

55

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 161:

5	AAGGAGCACC ACGAGAAACA CTCCAATTGG TGGAGTGTGA GCCGTGAGGG GTTCTCGTCT	60
	GTAGTGGACG AGGGCCGGGT GCACAAACAGC AGACAATCGC CAGACACACT ATTGGGCCCT	120
	GAGACAACAC TCGGCCGACT TTGGTCGACG TGGTGTCCCT CCATCTTGGT GGTGGGGTGT	180
10	GGTGTGAG CATTGAATAG TGGTTGCGAG CATCTAGACG GATGCGTTGC CCTCGGGCCG	240
	CGTGTTCGTC AAAAATGTGT AAATTTTTCT TTTGGTTTT GTGTTCGT	288

(2) INFORMATION FOR SEQ ID NO: 162:

15 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 289 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: cDNA

25 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 162:

30	AAGGAGCACC ACGAGAAACA CTCCAATTGG TGGAGTGTGA GCCGTGAGGG GTTCTCGTCT	60
	GTAGTGGACG GGAGCCGGGT GCACAAACAAC AGGCAATCGC CAGACACACT ATTGGGCCCT	120
	GAGACAACAC TCGGCCGGCT TTGAGTCGAA GTGGTGTCCC TCCATCTTGG TGGTGGGGTGT	180
35	TGGTGTGAG GCATTGAATA GTGGTTGCGA GCATCTAGAC GGATGCGTTG CCTTCGGGCC	240
	GCCTGTTCGT AAAAATGTGT TAATTTTTTC TTTTGGTTTT TGTGTTCGT	289

(2) INFORMATION FOR SEQ ID NO: 163:

40 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 232 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 163:

55	AGGGAGCACC GAAACGCATC CGCGTGGGG TGTGGGTTCG GCGTGTGTCG GCGTCGGCCG	60
----	--	----

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AGGTGTTGGG CAGCAGGCAG TAACCCCGGA ACACTGTTGG GTTTTGAGAA CACCCGTGGT 120
5 GGTGTTGTGC TCCCCGTGGT GCGGGGTGTG GTGTTGAGT GTGGATAGT GGTTGCGAGC 180
ATCTGGCAAA GACTGTGGTA AGCGGTTTTT GTTGATGTTT TCTGGTGTGTT GT 232

(2) INFORMATION FOR SEQ ID NO: 164:

10 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 279 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

15 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 164:

AAGGAGCACC ACGAGAAACA CTCCAATTGG TGGGGTGTGA GCCGTGAGGG GTTCTCGTCT 60
25 GTAGTGGACG AGGGCGGGTG CACAACAACA GCAATGCCA GACACACTAT TGCCCTGAG 120
ACAAACACTCG GCCGACTTGG TTGAAGTGGT GTCCCTCCAT CTTGGTGGTG GGGTGTGGTG 180
30 TTTGAGTATT GGATAGTGGT TGCGAGCATC TAATGAACGC GTCGCCGCAA CGGTTACGTG 240
TTCGTTTGT GTAATTTTC TATTGGTTTT TGTGTTCGT 279

(2) INFORMATION FOR SEQ ID NO: 165:

35 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 285 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 165:

AAGGAGCACC ACGAGAAACA CTCCAATTGG TGGGGTGTGA GCCGTGAGGG GTTCTCGTCT 60
50 GTAGTGGACG AGGGCCGGGT GCACAAACAAG AGGCAATCGC CAGACACACT ATGGCCCTG 120
AGACAAACACT CGGCCGACTT TGGTCGAAGT GGTGTCCCCC CATCTTGGTG GTGGGGTGTG 180
55 GTGTTGAGT ATTGGATAGT GGTTGCGAAC ATCTAAATGA ACGCGTTGCC GGCAACGGTT 240
ACGTGTTCGT TTTAGTGTAA TTTTCTAAT GGTTTTGTG TTCGT 285

(2) INFORMATION FOR SEQ ID NO: 166:

5 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 384 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

10 (ii) MOLECULE TYPE: cDNA

 (iii) HYPOTHETICAL: NO

15 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 166:

AAGGAGCACC ACGAGACCTG GGCGGGCCCC GCAGATCGCG GGATCAGCTG AGCTTCAGG	60
CGATTCGTTG GATGGCCTCG CACCTGTAGT GGGTGGGGGT CTGGTGCACT CAACAAACTT	120
GGCGTGGGAT GCGGGAAAGC ATCTGCGGAA AATCATCAGA CACACTATTG GGCTTGAGA	180
CAACAGGCC GCAGCCTGCC CGTTGGGGGC AGGGGTGTGT TGTTGCCTCA CTTTGGTGGT	240
GGGGGTGGTG TTTGATTTGT GGATAGTGGT TCCGAGCATC TAGCGCGCAG AATGTGTGGT	300
CTCACTCCTT GTGGGTGGGG CCTGGTTTG TGTGCGATTG ATGTGCAATT TCTTTGAAA	360
CTCATTTTTG GTTTTTGTG TTGT	384

(2) INFORMATION FOR SEQ ID NO: 167:

35 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 295 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: cDNA

 (iii) HYPOTHETICAL: NO

 (iii) ANTI-SENSE: NO

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 167:

AAGGAGCACC ACGAAAAACT CCCCAATTGG TGGGGTGTAA GCCGTGAGGG GTTCCCGTCT	60
GTAGTGGACG GGGGCCGGGT GCGAACAGC AAGCGAAACG CCGGACACAC TATTGGTCC	120
TGAGGCAACA CTCGGGTTTG TCCCCCTCAG GGATTTCTG GGTGTTGTCC CACCATCTTG	180
GTGGTGGGGT GTGGTGTGGT AGAATTGGAT AGTGGTTGCG AGCATCAAAT GGATGCGTTG	240
CCCCCTACGGG TAGCGTGTTC TTTTGTGCAA TTTTATTCTT GGTTTTGTG TTTGT	295

(2) INFORMATION FOR SEQ ID NO: 168:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 279 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 168:

AAGGAGCACC ACGAGAACCA CTCCAACCTGG TGGGGTGCAA GCCGTGAGGG GTTCTCGTCT	60
GTAGTGGACG AGAGCCGGGT GCGCGACAAAC GAACGAGCCA GACACACTAT TGGGTCCCTGA	120
GGCAACACTC GGGCTTGGCC AGAGCTGTTG TCCCACCATC TTGGTGGTGG GGTGTGGTGT	180
TTGAGAATTG GATACTGGTT GCGAGCATCA AATGGATGCG TTGCCCTAC GGGTGGCGTG	240
TTCTTTGTG CAAATTTATT CTTTGGTTTT TGTGTTTGT	279

(2) INFORMATION FOR SEQ ID NO: 169:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 286 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 169:

AAGGAGCACC ACGAAAAACA CCCCAACTGG TGGGGTGAA GCCGTGAGGG GCTCCCGTCT	60
GTAGTAGACG GGCGCCGGGT GCGAACAGC AAGCGAGCCA GACACACTAT TGGGTCCCTGA	120
GGCAACACTC GGGCTTGTCT TGGACTCGTC CAAGAGTGTGTT GTCCCACCAT CTTGGTGGTGT	180
GGGTGTGGTG TTTGAGAATT GGATAGTGGT TGCGAGCATC ACTGGATGCG TTGCCCCAG	240
GGGTAGCGTG TTCTTTGTG CAAATTTATTC TGGTTTTGT GTTAGT	286

(2) INFORMATION FOR SEQ ID NO: 170:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 265 base pairs
- (B) TYPE: nucleic acid

(C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 170:

AAGGAGCACC ACGAAAAACA CTCCGCATCC GGTGGGGTGT GAGCCGTGAG GGAGCCCGTG	60
CCTGTAGTGG GTGTGGGTTG GGTGCGCGAC AACAAATGGG AAAAATCGCT GGGCACACTA	120
TTGGGCTTTG AGGCAACACC TGGTTTGTTC TGGGTGGTGT CGCTCCATCT TGGTGGTGGG	180
GTGTGGTGTGTT TGAGTTGTGG ATAGTGGTTG CGAGCATCTA AGCAAAAGCT GTTGTGGTAC	240
GGTTTTGTC GAGTGTGTG TGTGT	265

20

(2) INFORMATION FOR SEQ ID NO: 171:

25 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 299 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

30

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 171:

AAGGAGCACC ACGAAAAACA CTCCAATTGG TGGGTGTAA GCCGTGAGGG GTTCTCATCT	60
GTAGTGGACG AGAGCCGGGT GCACAAACAGC AAATGAATCG CCAGACACAC TGTGGGTCC	120
TGAGGCAACA CTCAGGCTTG TCCCATGTTG GGCTTGATCG GGTGCTGTCC CCCCATCTTG	180
GTGGTGGGGT GTGGTGTGTT AGTATTGGAT AGTGGTTGCG AGCATCTAAA TGGATAACGTT	240
GCCAGTAATG GTGGCGTATT CATTGAAAAT GTGTAATTTC CTTCTTTGGT TTTGTGTGT	299

45

(2) INFORMATION FOR SEQ ID NO: 172:

50 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 299 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

55

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 172:

10	AAGGAGCACC ACGAAAAACA CTCCAATTGG TGGGGTGTAA GCCGTGAGGG GTTCTCATCT	60
	GTAGTGGACG AGAGCCGGGT GCACAAACAGC AAATGAATCG CCAGACACAC TGTTGGGTCC	120
	TGAGGCAACA CTCAGGCTTG TCCCAGTGTG GGCTTGATCG GGTGCTGTCC CCCCATCTTG	180
15	GTGGTGGGGT GTGGTGTGTTG AGTATTGGAT AGTGGTTGCG AGCATCTAAA TGGATAACGTT	240
	GCCAGTAATG GTGGCGTGTGTT CATTGAAAAT GTGTAATTTC TTCTTTGGT TTTGTGTGT	299

(2) INFORMATION FOR SEQ ID NO: 173:

20 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 298 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

30 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 173:

35	AAGGAGCACC ACGAAAAACA CTCCAATTGG TGGGGTGTAA GCCGTGAGGG GTTCTCATCT	60
	GTAGTGGACG AGAGCCGGGT GCACAAACAGC AAATGAATCG CCAGACACAC TGTTGGGTCC	120
	TGAGGCAACA CTCAGGCTTG TCCCAGTGTG GGCTTGATCG GGTGCTGTCC CCCCATCTTG	180
40	GTGGTGGGGT GTGGTGTGTTG AGTATTGGAT AGTGGTTGCG AGCATCTAAA TGGAACGTTG	240
	CCAGTAATGG TGGCGTGTTC ATTGAAAATG TGTAATTTC TTCTTIGGTT TTGTGTGT	298

(2) INFORMATION FOR SEQ ID NO: 174:

45 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 300 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

50 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 174:

5	AAGGAGCACC ATTTCTCAGT CGAATGAAC T GAGAACATAA AGCGAGTATC TGTAGTGGAT	60
	ACATGCTTGG TGAATATGTT TTATAAAATCC TGTCCACCCC GTGGATAGGT AGTCGGCAAA	120
	ACGTCGGACT GTCATAAGAA TTGAAACGCT GGCACACTGT TGGGTCTGA GGCAACACAT	180
10	TGTGTTGTCA CCCTGCTTGG TGGTGGGTG TGGTCCTTGA CTTATGGATA GTGGTTGCGA	240
	GCATCTAAAC ATAGCCTCGC TCGTTTCGA GTGAGGCTGG TTTTGCAAT TTTATTAGCT	300

(2) INFORMATION FOR SEQ ID NO: 175:

15 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 22 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

25 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 175:

30	GGTTTCGGGA TGTTGTCCCA CC	22
----	--------------------------	----

(2) INFORMATION FOR SEQ ID NO: 176:

35 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 21 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 176:
 CGACTGAGGT CGACGTGGTG T

(2) INFORMATION FOR SEQ ID NO: 177:

50 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 27 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

5 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 177:

GGTGTGAG CATTGAATAG TGGTTGC

27

(2) INFORMATION FOR SEQ ID NO: 178:

15 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

25 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 178:

30 GTTGGGCAGC AGGCAGTAAC C

21

(2) INFORMATION FOR SEQ ID NO: 179:

35 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

40 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 179:

CCGGCAACGG TTACGTGTTTC

20

(2) INFORMATION FOR SEQ ID NO: 180:

50 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

55

(ii) MOLECULE TYPE: cDNA

5 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 180:

TCGTTGGATG GCCTCGCACC T

21

(2) INFORMATION FOR SEQ ID NO: 181:

15 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 181:

ACTTGGCCTG GGATGCAGGA A

21

30 (2) INFORMATION FOR SEQ ID NO: 182:

35 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

40 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 182:

CCCTCAGGGA TTTTCTGGGT GTTG

24

(2) INFORMATION FOR SEQ ID NO: 183:

50 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

55 (ii) MOLECULE TYPE: cDNA

5 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 183:

15 CGACTCGTCC AAGAGTGTTG TCC

23

(2) INFORMATION FOR SEQ ID NO: 184:

20 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: cDNA

20 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 184:

TCGGGGCTTGG CCAGAGCTGT T

21

30 (2) INFORMATION FOR SEQ ID NO: 185:

35 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

40 (iii) ANTI-SENSE: NO

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 185:

GGGTGCGCAA CAGCAAGCGA

20

(2) INFORMATION FOR SEQ ID NO: 186:

50 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 19 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

55 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 186:

GATGCGTTGC CCCTACGGG

19

10

(2) INFORMATION FOR SEQ ID NO: 187:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 24 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

20

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 187:

CCCTACGGGT AGCGTGTTCT TTTG

24

30

(2) INFORMATION FOR SEQ ID NO: 188:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 23 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

35

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

40

(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 188:

45

CGGATCGATT GAGTGCTTGT CCC

23

(2) INFORMATION FOR SEQ ID NO: 189:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 23 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

50

(ii) MOLECULE TYPE: cDNA

55

(iii) HYPOTHETICAL: NO

5
(iii) ANTI-SENSE: NO

10
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 189:
TCTAAATGAA CGCACTGCCG ATG

23

15
(2) INFORMATION FOR SEQ ID NO: 190:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

20
(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

25
(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 190:

TGAGGGAGCC CGTGCCTGTA

20

30
(2) INFORMATION FOR SEQ ID NO: 191:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

35
(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

40
(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 191:

CATGTTGGGC TTGATCGGGT GC

22

45
(2) INFORMATION FOR SEQ ID NO: 192:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

50
(ii) MOLECULE TYPE: cDNA

55
(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 192:

CCTGGGTTTG ACATGCACAG

20

10 (2) INFORMATION FOR SEQ ID NO: 193:

15 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

20 (iii) ANTI-SENSE: NO

25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 193:

26 GCGTAGTAGC GTTTCGCTCG G

21

(2) INFORMATION FOR SEQ ID NO: 194:

30 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

35 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 194:

41 CGCAAGAACG TTGCTCAAGC C

21

45 (2) INFORMATION FOR SEQ ID NO: 195:

50 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 470 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

55 (iii) ANTI-SENSE: NO

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 195:

	CCTAATGATA TTGATTGCGC TGAAGTGCTC ACACAGATTG TCTGATGAAA AAGTAACGAG	60
10	CAGAAATACC TTTATAGGCT TGTAGCTCAG GTGGTTAGAG CGCACCCCTG ATAAGGGTGA	120
	GGTCGGTGGT TCAAGTCCAC TCAGGCCTAC CACTTCTCGA AGTGGAAAAG GTACTGCACG	180
	TGACTGTATG GGGCTATAGC TCAGCTGGGA GAGCGCCTGC CTTGCACGCA GGAGGTCAGC	240
15	GGTCGATCC CGCTTAGCTC CACCATATAG TCCTGTATT CAATACTTCA GAGTGTACTG	300
	GCAACAGTAT GCTGCGAAGT ATTTTGCTCT TTAACAATCT GGAACAAAGCT GAAAATTGAA	360
	ACATGACAGC TGAAACTTAT CCCTCCGTAG AAGTATTGGG GTAAGGATTA ACCTGTCATA	420
20	GAGTCTCTCA AATGTAGCAG CACGAAAGTG GAAACACCTT CGGGTTGTGA	470

(2) INFORMATION FOR SEQ ID NO: 196:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 453 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 196:

	CCTAATGATA TTGATTGCGC TGAAGTGCTC ACACAGATTG TTTGATAGAA ACGTAATGAG	60
40	CAAAGCGCT ACCTGTTGAT GTAATGAGTC ACTGACTCAT GCTGATACGA ACCGATTAAG	120
	ACAGTCAGTT TAATCGGATT TTCGTGTCCT CATCGTCTAG AGGCCTAGGA CACTGCCCTT	180
	TCACGGCTGT AACAGGGGTT CGAACCCCT TGGGGACGCC ATTGATAAT GAGTGAAAGA	240
45	CATTATCACC GGTTCTTGGA ACCGAAAACA TCTTAAAGAT GACTCTGCG AGTCGTGTTT	300
	AAGATATTGC TCTTTAACAA TCTGGAACAA GCTGAAAATT GAAACATGAC AGCTGAAACT	360
	TATCCCTCCG TAGAAGTATT GGGGTAAGGA TTAACCTGTC ATAGAGTCTC TCAAATGTAG	420
50	CAGCACGAAA GTGGAAACAC CTTCGGGTTG TGA	453

(2) INFORMATION FOR SEQ ID NO: 197:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 248 base pairs
- (B) TYPE: nucleic acid

- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 197:

TAAGGATAAAG GAAGAAGCCT GAGAAGGTTT CTGACTAGGT TGGGCAAGCA TTTATATGTA 60
AGAGCAAGCA TTCTATTCA TTTGTGTTGT TAAGAGTAGC GCGGTGAGGA CGAGACATAT 120
AGTTTGATGAT CAAGTATGTT ATTGTAAAGA AATAATCATG GTAACAAGTA TATTCACGC 180
ATAATAATAG ACGTTTAAGA GTATTTGTCT TTTAGGTGAA GTGCTTGCAT GGATCTATAG 240
AAATTACA 248

(2) INFORMATION FOR SEQ ID NO: 198:

25 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 198:

GGAAAAGGTA CTGCACGTGA CTG

23

⁴⁰ (2) INFORMATION FOR SEQ ID NO: 188.

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 23 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

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(xii) SEQUENCE DESCRIPTION: SEQ ID NO: 188

GACAGCTGAA ACTTATCCCT CCG

23

(2) INFORMATION FOR SEQ ID NO: 200:

5 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 25 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

10 (ii) MOLECULE TYPE: cDNA

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 200:

GCTACCTGTT GATGTAATGA GTCAC

25

(2) INFORMATION FOR SEQ ID NO: 201:

20 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 22 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

30 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 201:

GAGTAGCGCG GTGAGGGACCA GA

22

(2) INFORMATION FOR SEQ ID NO: 202:

35 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 25 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 202:

CTTTTATGTC AGATAAAAGTA TGCAA

25

(2) INFORMATION FOR SEQ ID NO: 203:

55 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 22 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

5 (D) TOPOLOGY: LINE
 (ii) MOLECULE TYPE: cDNA
10 (iii) HYPOTHETICAL: NO
 10 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 203:

CGTAAAAAGGG TATGATTATT TG 22

(2) INFORMATION FOR SEO ID NO: 204:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 204:

TCGAGAATTG GAAAGAGGTC 20

35 (2) INFORMATION FOR SEQ ID NO: 205:

(1) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 19 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: cDNA
(iii) HYPOTHETICAL: NO
(iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 205:

AAGAGGTCGG ATTTATCCG 19

(2) INFORMATION FOR SEQ ID NO: 206:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs

(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

10 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 206:

15 TTTCGACTGCA AATGCTCG

18

(2) INFORMATION FOR SEQ ID NO: 207:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 19 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

25 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 207:

TCTTAAAGCC GCATTATGC

19

(2) INFORMATION FOR SEQ ID NO: 208:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

45 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 208:

50 CCTAAATGATA TTGATTTCGCG

20

(2) INFORMATION FOR SEQ ID NO: 209:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid

(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 209:

ATGACAGGTT AATCCTTACC CC

22

15 (2) INFORMATION FOR SEQ ID NO: 210:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 25 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

25

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 210:

GGTGTTGGTCC TTGACTTATG GATAG

25

(2) INFORMATION FOR SEQ ID NO: 211:

35

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

40

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 211:

50

TCGGGCCGCG TGTTCGTCAA A

21

(2) INFORMATION FOR SEQ ID NO: 212:

55

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 24 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

5 (iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 212:

CGTTTCATA AGCGATCGCA CGTT

24

15 (2) INFORMATION FOR SEQ ID NO: 213:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 235 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

25 (iii) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 213:

30 TAAGGATAAG GAAACCTGTG AATCTTTTC CCTTCTTTG TTCAGTTTG AGAGGTTCAT

60

CTCTCAAAAC GTGTTCTTG AAAACTAGAT AAGAAAAGTT AGTGTAAAAA GACGAAGAGA

120

AACCGTAGGT TTTTCTTCAA CCAAAACCGA GAATCAAACC GAGAAAGAAT CTTTCCGTTT

180

35 TCATAAGCGA TCGCACGTT ATGAAAACAC AACAAACACCT TCGTAAGAAG GATGA

235

(2) INFORMATION FOR SEQ ID NO: 214:

40 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 475 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iii) ANTI-SENSE: NO

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 214:

TAAGGATAAG GAAACCTGTG AATCTTTTC CCTTCTTTG TTCAGTTTG AGAGGTCAT

60

55 GACGCTCATA CTGAGTACCA GGTGACACGT TTTTGAGGTG TCTCTTCGTA TGAGGGGCCT

120

	ATAGCTCAGC TGGTTAGAGC GCACGCCTGA TAAGCGTGAG GTCGGTGGTT CGAGTCCACT	180
5	TAGGCCCACT TTTTGAAATA AACCTTCCTT TTTTATATGT TAATAAGGGG CCTTAGCTCA	240
	GCTGGGAGAG CGCCTGCTTT GCACGCAGGA GGTCAAGCGGT TCGATCCCAC TAGGCTCCAC	300
	CAAAGATAGT TTGTTCTTG AAAACTAGAT AAGAAAAGTT AGTGTAAAAA GACGAAGAGA	360
10	AACCGTAGGT TTTTCTTCAA CCAAAACCGA GAATCAAACC GAGAAAGAAT CTTCCGTTT	420
	TCATAAAGCGA TCGCACGTTT ATGAAAACAC ACAACACCT TCGTAAGAAG GATGA	475

(2) INFORMATION FOR SEQ ID NO: 215:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 463 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 215:

30	TAAGGATAAG GAAACCTGTG AATCTTTTC CCTTCTTTG TTCAGTTTG AGAGGTCAAT	60
	GACGCTCATA CTGAGTACCA GGTGACACGT TTTTGAGGTG TCTCTCGTA TGAGGGCCT	120
	ATAGCTCAGC TGGTTAGAGC GCACGCCTGA TAAGCGTGAG GTCGGTGGTT CGAGTCCACT	180
35	TAGGCCCACT TTTTGAAATA AACCTTCCTT TTTTATATGT TAATAAGGGG CCTTAGCTCA	240
	GCTGGGAGAG CGCCTGCTTT GCACGCAGGA GGTCAAGCGGT TCGATCCCAC TAGGCTCCAC	300
	CAAAGATAGT TTGTTCTTG AAAACTAGAT AAGAAAAGTT AGTGTAAAAA GACGAAGAGA	360
40	AACCGTAGGT TTTTCTTCAA CCAAAACCGA GAAAGAATCT TTCCGTTTC ATAAGCGATC	420
	GCACGTTAT GAAAACACAA CAACACCTTC GTAAGAAGGA TGA	463

(2) INFORMATION FOR SEQ ID NO: 216:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 19 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 216:

TGGCCGGTGC AAAGGGCTG

19

10 Claims

15 1. Method for the detection and identification of at least one strain of Mycobacterium species or for the simultaneous detection of several microorganisms of which at least one strain of Mycobacterium species in a sample, comprising the steps of:

20 (i) releasing, isolating and/or concentrating the polynucleic acids from the microorganism(s) to be detected in the sample;

(ii) if need be amplifying the 16S-23S rRNA spacer region, or a part of it, from the microorganism(s) to be detected, with at least one suitable primer pair;

(iii) hybridizing the polynucleic acids of step (i) or (ii) to at least one of the following probes:

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	MYC-ICG-1 :	ACTGGATAGTGGTTGCGAGCATCTA	(SEQ ID NO 1)
5	MYC-ICG-22 :	CTTCTGAATAGTGGTTGCGAGCATCT	(SEQ ID NO 2)
	MTB-ICG-1 :	GGGTGCATGACAACAAAGTTGGCCA	(SEQ ID NO 3)
	MTB-ICG-2 :	GACTTGTCCAGGTGTTGTCCCAC	(SEQ ID NO 4)
10	MTB-ICG-3 :	CGGCTAGCGGTGGCGTGTCT	(SEQ ID NO 5)
	MAI-ICG-1 :	CAACAGCAAATGATTGCCAGACACAC	(SEQ ID NO 6)
	MIL-ICG-11 :	GAGGGGTTCCCGTCTGTAGTG	(SEQ ID NO 7)
15	MIL-ICG-22 :	TGAGGGGTTCTCGTCTGTAGTG	(SEQ ID NO 8)
	MAC-ICG-1 :	CACTCGGTCGATCCGTGTGGA	(SEQ ID NO 9)
	MAV-ICG-1 :	TCGGTCCGTCCGTGTGGAGTC	(SEQ ID NO 10)
20	MAV-ICG-22 :	GTGGCCGGCGTTCATCGAAA	(SEQ ID NO 11)
	MIN-ICG-1 :	GCATAGTCCTAGGGCTGATGCGTT	(SEQ ID NO 12)
	MIN-ICG-2 :	GCTGATGCGTTCGTCGAAATGTGTA	(SEQ ID NO 13)
25	MIN-ICG-22 :	CTGATGCGTTCGTCGAAATGTGT	(SEQ ID NO 14)
	MIN-ICG-222 :	TGATGCGTTCGTCGAAATGTGT	(SEQ ID NO 15)
	MIN-ICG-2222 :	GGCTGATGCGTTCGTCGAAATGTGTAA	(SEQ ID NO 16)
30	MAL-ICG-1 :	ACTAGATGAACCGCGTAGTCCTTGT	(SEQ ID NO 17)
	MHEF-ICG-1 :	TGGACGAAAACCGGGTGCACAA	(SEQ ID NO 18)
	MAH-ICG-1 :	GTGTAATTCTTTTAACCTTGTGTAAAGTAAGTG	
35			(SEQ ID NO 19)
	MCO-ICG-11 :	TGGCCGGCGTGTTCATCGAAA	(SEQ ID NO 20)
40	MTH-ICG-11 :	GCACTTCAATTGGTGAAGTGCAGGCC	(SEQ ID NO 21)

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MTH-ICG-2 :	GCGTGGTCTTCATGGCCGG	(SEQ ID NO 22)
MEF-ICG-11 :	ACGCGTGGTCCTTCGTGG	(SEQ ID NO 23)
5 MSC-ICG-1 :	TCGGCTCGTCTGAGTGGTGT	(SEQ ID NO 24)
MKA-ICG-1 :	GATGCCTTGCTACGGTAGCGT	(SEQ ID NO 25)
10 MKA-ICG-2 :	GATGCCTGCCTACGGTAGCGT	(SEQ ID NO 26)
MKA-ICG-3 :	ATGCGTTGCCCTACGGTAGCGT	(SEQ ID NO 27)
MKA-ICG-4 :	CGGGCTCTGTCGAGAGTTGT	(SEQ ID NO 28)
15 MKA-ICG-5 :	CCCTCAGGGATTTCTGGGTGTG	(SEQ ID NO 182)
MKA-ICG-6 :	GGACTCGTCCAAGAGTGTGTCC	(SEQ ID NO 183)
MKA-ICG-7 :	TCGGGCTTGGCCAGAGCTGTT	(SEQ ID NO 184)
20 MKA-ICG-8 :	GGGTGCGAACAGCAAGCGA	(SEQ ID NO 185)
MKA-ICG-9 :	GATGCCTGCCCTACGGG	(SEQ ID NO 186)
MKA-ICG-10 :	CCCTACGGTAGCGTGTCTTTG	(SEQ ID NO 187)
25 MCH-ICG-1 :	GGTGTGGACTTGACTTCTGAATAG	(SEQ ID NO 29)
MCH-ICG-2 :	CGGAAAACGTCGGACTGTCA	(SEQ ID NO 30)
MGO-ICG-1 :	AACACCCTGGGTGCTGTCC	(SEQ ID NO 31)
30 MGO-ICG-2 :	GTATGCCTGTCGTCGCGGC	(SEQ ID NO 32)
MGO-ICG-5 :	CGTGAGGGTCATCGTCTGTAG	(SEQ ID NO 33)
MUL-ICG-1 :	GGTTTCGGGATGTTGTCCCACC	(SEQ ID NO 175)
35 MGV-ICG-1 :	CGACTGAGGTCGACGTGGTGT	(SEQ ID NO 176)
MGV-ICG-2 :	GGTGTGAGCATTGAATAGTGGTTGC	(SEQ ID NO 177)
MXE-ICG-1 :	GTTGGCAGCAGGCAGTAACC	(SEQ ID NO 178)
40 MSI-ICG-1 :	CCGGCAACGGTACGTGTT	(SEQ ID NO 179)
MFO-ICG-1 :	TCGTTGGATGGCCTCGCACCT	(SEQ ID NO 180)
45 MFO-ICG-2 :	ACTTGGCGTGGGATGCGGGAA	(SEQ ID NO 181)
MML-ICG-1 :	CGGATCGATTGAGTGCTTGTCCC	(SEQ ID NO 188)
MML-ICG-2 :	TCTAAATGAACGCAGTGCCTGATGG	(SEQ ID NO 189)
50 MCE-ICG-1 :	TGAGGGAGCCCGTGCCTGTA	(SEQ ID NO 190)
MHP-ICG-1 :	CATGTTGGCTTGATCGGGTGC	(SEQ ID NO 191)

55 or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 76-110, or 157-174 provided said probe hybridizes specifically to a Mycobacterium species.

(iv) detecting the hybrids formed in step (iii);

(v) identification of the micro-organism(s) present in the sample from the differential hybridization signals ob-

tained in step (iv).

2. Method according to claim 1, to detect and identify one or more Mycobacterium tuberculosis complex strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

5	MTB-ICG-1 :	GGGTGCATGACAACAAAGTTGGCCA	(SEQ ID NO 3)
10	MTB-ICG-2 :	GACTTGTCCAGGTGTTGTCCCAC	(SEQ ID NO 4)
15	MTB-ICG-3 :	CGGCTAGCGGTGGCGTGTCT	(SEQ ID NO 5)

or to equivalents of said probes,
and/or to any probe derived from SEQ ID NO 76 provided said probe hybridizes specifically to the M. tuberculosis complex.

20 3. Method according to claim 1 to detect and identify one or more Mycobacterium strains from the MAIS-complex, wherein step (iii) comprises hybridizing to at least one of the following probes:

25	MAI-ICG-1 :	CAACAGCAAATGATTGCCAGACACAC	(SEQ ID NO 6)
30	MIL-ICG-11 :	GAGGGGTTCCCGTCTGTAGTG	(SEQ ID NO 7)
35	MIL-ICG-22 :	TGAGGGGTTCTCGTCTGTAGTG	(SEQ ID NO 8)
40	MAC-ICG-1 :	CACTCGGTGATCCGTGTGGA	(SEQ ID NO 9)
45	MAV-ICG-1 :	TCGGTCCGTCGGTGGAGTC	(SEQ ID NO 10)
50	MAV-ICG-22 :	GTGGCCGGCGTTCATCGAAA	(SEQ ID NO 11)
55	MIN-ICG-1 :	GCATAGTCCTAGGGCTGATGCGTT	(SEQ ID NO 12)
60	MIN-ICG-2 :	GCTGATGCGTTCGTCGAAATGTGTA	(SEQ ID NO 13)
65	MIN-ICG-22 :	CTGATGCGTTCGTCGAAATGTGT	(SEQ ID NO 14)
70	MIN-ICG-222 :	TGATGCGTTCGTCGAAATGTGT	(SEQ ID NO 15)
75	MIN-ICG-2222 :	GGCTGATGCGTTCGTCGAAATGTGTAA	(SEQ ID NO 16)
80	MAL-ICG-1 :	ACTAGATGAACCGCGTAGTCCTTGT	(SEQ ID NO 17)
85	MHEF-ICG-1 :	TGGACGAAAACCGGGTGCACAA	(SEQ ID NO 18)
90	MAH-ICG-1 :	GTGTAATTCTTTTAACCTTGTGTAAAGTAAGTG	(SEQ ID NO 19)
95	MCO-ICG-11 :	TGGCCGGCGTGTTCATCGAAA	(SEQ ID NO 20)
100	MTH-ICG-11 :	GCACTTCAATTGGTGAAGTGCAGGCC	(SEQ ID NO 21)
105	MTH-ICG-2 :	GCGTGGTCTTCATGGCCGG	(SEQ ID NO 22)
110	MEF-ICG-11 :	ACGCGTGGTCCTCGTGG	(SEQ ID NO 23)
115	MSC-ICG-1 :	TCGGCTCGTTCTGAGTGGTGT	(SEQ ID NO 24)

or to equivalents of said probes,
and/or to any probe derived from SEQ ID NO 77-100 or 108-110, provided said probe hybridizes specifically to strains from the MAIS complex.

5 4. Method according to claim 1 to detect and identify one or more M. avium and M. paratuberculosis strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

10 MAV-ICG-1 : TCGGTCCGTCCGTGTGGAGTC (SEQ ID NO 10)
MAV-ICG-22 : GTGGCCGGCGTTCATCGAAA (SEQ ID NO 11)

or to equivalents of said probes,
and/or to any probe derived from SEQ ID NO 77 and 78 provided said probe hybridizes specifically to M. avium
15 or M. paratuberculosis.

20 5. Method according to claim 1 to detect and identify one or more Mycobacterium intracellulare strains and MIC-
strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

25 MAI-ICG-1 : CAACAGCAAATGATTGCCAGACACAC (SEQ ID NO 6)

MIL-ICG-11 : GAGGGGTTCCCGTCTGTAGTG (SEQ ID NO 7)

30 MIL-ICG-22 : TGAGGGGTTCTCGTCTGTAGTG (SEQ ID NO 8)

MAC-ICG-1 : CACTCGGTGATCCGTGTGGA (SEQ ID NO 9)

MIN-ICG-1 : GCATAGTCCTAGGGCTGATGCGTT (SEQ ID NO 12)

35 MIN-ICG-2 : GCTGATGCGTTCGTCGAAATGTGTA (SEQ ID NO 13)

MIN-ICG-22 : CTGATGCGTTCGTCGAAATGTGT (SEQ ID NO 14)

MIN-ICG-222 : TGATGCGTTCGTCGAAATGTGT (SEQ ID NO 15)

35 MIN-ICG-2222 : GGCTGATGCGTTCGTCGAAATGTGTAA (SEQ ID NO 16)

MAL-ICG-1 : ACTAGATGAACGCGTAGTCCTTGT (SEQ ID NO 17)

MHEF-ICG-1 : TGGACGAAAACC GG GTGCACAA (SEQ ID NO 18)

40 MAH-ICG-1 : GTGTAATTCTTTAACTCTTGTGTAAAGTAAGTG (SEQ ID NO 19)

MCO-ICG-11 : TGGCCGGCGTGTTCATCGAAA (SEQ ID NO 20)

45 MTH-ICG-11 : GCACTTCAATTGGTGAAGTGCAGGCC (SEQ ID NO 21)

MTH-ICG-2 : GCGTGGTCTTCATGGCCGG (SEQ ID NO 22)

50 MEF-ICG-11 : ACGCGTGGTCCTCGTGG (SEQ ID NO 23),

55 or to equivalents of said probes,
and/or to any probe derived from SEQ ID NO 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96,
97, 98 or 99 provided said probe hybridizes specifically to M. intracellulare strains and MIC-strains.

6. Method according to claim 1 to detect and identify one or more Mycobacterium intracellulare strains in a sample,
wherein step (iii) comprises hybridizing to the following probe:

MIN-ICG-1 : GCATAGTCCTTAGGGCTGATGCGTT

(SEQ ID NO 12),

or to equivalents of said probe,

5 and/or to any probe derived from SEQ ID NO 89 provided said probe hybridizes specifically to M. intracellulare.

7. Method according to claim 1 to detect and identify one or more Mycobacterium scrofulaceum strains in a sample, wherein step (iii) comprises hybridizing to the following probe:

10 MSC-ICG-1 : TCGGCTCGTTCTGAGTGGTGTC

(SEQ ID NO 24),

or to equivalents of said probe,

15 and/or to any probe derived from SEQ ID NO 100 provided said probe hybridizes specifically to M. scrofulaceum.

8. Method according to claim 1 to detect and identify one or more Mycobacterium kansasii strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

20 MKA-ICG-1 : GATGCGTTGCTACGGGTAGCGT

(SEQ ID NO 25)

MKA-ICG-2 : GATGCGTTGCCTACGGGTAGCGT

(SEQ ID NO 26)

MKA-ICG-3 : ATGCGTTGCCCTACGGGTAGCGT

(SEQ ID NO 27)

25 MKA-ICG-4 : CGGGCTCTGTTCGAGAGAGTTGTC

(SEQ ID NO 28)

MKA-ICG-5 : CCCTCAGGGATTTCTGGGTGTTG

(SEQ ID NO 182)

MKA-ICG-6 : GGACTCGTCCAAGAGTGTGTTG

(SEQ ID NO 183)

30 MKA-ICG-7 : TCAGGGCTTGGCCAGAGCTGTT

(SEQ ID NO 184)

MKA-ICG-8 : GGGTGCGCAACAGCAAGCGA

(SEQ ID NO 185)

MKA-ICG-9 : GATGCGTTGCCCTACGGG

(SEQ ID NO 186)

MKA-ICG-10 : CCCTACGGGTAGCGTGTCTTTG

(SEQ ID NO 187)

40 or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 101, 167, 168, or 169 provided said probe hybridizes specifically to M. kansasii.

45 9. Method according to claim 1 to detect and identify one or more Mycobacterium chelonae strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

50 MCH-ICG-1 : GGTGTGGACTTGACTTCTGAATAG

(SEQ ID NO 29)

MCH-ICG-2 : CGGCAAAACGTCGGACTGTCA

(SEQ ID NO 30)

55 MCH-ICG-3 : GGTGTGGTCCTGACTTATGGATAG

(SEQ ID NO 210)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 102, 103 or 174 provided said probe hybridizes specifically to M. chelonae.

10. Method according to claim 1 to detect and identify one or more Mycobacterium gordonaiae strains in a sample.

wherein step (iii) comprises hybridizing to at least one of the following probes:

MGO-ICG-1 : AACACCCTCGGGTGCTGTCC (SEQ ID NO 31)

MGO-ICG-2 : GTATGCGTTGTCGTCGCGGC (SEQ ID NO 32)

MGO-ICG-5 : CGTGAGGGGTACCGTCTGTAG (SEQ ID NO 33)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 104, 105 or 106 provided said probe hybridizes specifically to M. gordoneae.

11. Method according to claim 1 to detect and identify one or more Mycobacterium ulcerans strains or M. marinum strains in a sample, wherein step (iii) comprises hybridizing to the following probe:

MUL-ICG-1 : GGTTTCGGGATGTTGTCCCACC (SEQ ID NO 175)

or to equivalents of said probe,

and/or to any probe derived from SEQ ID NO 157 provided said probe hybridizes specifically to M. ulcerans and M. marinum.

12. Method according to claim 1 to detect and identify one or more Mycobacterium genavense strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

MGV-ICG-1 : CGACTGAGGTCGACGTGGTGT (SEQ ID NO 176)

MGV-ICG-2 : GGTGTTGAGCATTGAATAGTGGTTGC (SEQ ID NO 177)

MGV-ICG-3 : TCGGGCCCGCGTGTTCGTAAA (SEQ ID NO 211)

or to equivalents of said probes,

and/or to any probe derived from SEQ ID NO 158, 159, 160, 161 or 162 provided said probe hybridizes specifically to M. genavense.

13. Method according to claim 1 to detect and identify one or more Mycobacterium xenopi strains in a sample, wherein step (iii) comprises hybridizing to the following probe:

MXE-ICG-1 : GTTGGGCAGCAGGCAGTAACC (SEQ ID NO 178)

or to equivalents of said probe,

and/or to any probe derived from SEQ ID NO 163, provided said probe hybridizes specifically to M. xenopi.

14. Method according to claim 1 to detect and identify one or more Mycobacterium simiae strains in a sample, wherein step (iii) comprises hybridizing to the following probe:

MSI-ICG-1 : CCGGCAACGGTTACGTGTTTC (SEQ ID NO 179)

or to equivalents of said probe,

and/or to any probe derived from SEQ ID NO 164 or 165 provided said probe hybridizes specifically to M. simiae.

15. Method according to claim 1 to detect and identify one or more Mycobacterium fortuitum strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

MFO-ICG-1 : TCGTTGGATGCCCTCGCACCT (SEQ ID NO 180)
MFO-ICG-2 : ACTTGGCGTGGGATGCAGGAA (SEQ ID NO 181)

5 or to equivalents of said probes,
and/or to any probe derived from SEQ ID NO 166, provided said probe hybridizes specifically to *M. fortuitum*.

16. Method according to claim 1 to detect and identify one or more Mycobacterium celatum strains in a sample, wherein
step (iii) comprises hybridizing to the following probe:

MCE-ICG-1 : TGAGGGAGCCCCGTGCCTGTA (SEQ ID NO 190)

15 or to equivalents of said probe,
and/or to any probe derived from SEQ ID NO 170, provided said probe hybridizes specifically to *M. celatum*.

17. Method according to claim 1 to detect and identify one or more *Mycobacterium haemophilum* strains in a sample, wherein step (iii) comprises hybridizing to the following probe:

20

MHP-ICG-1 : CATGTTGGGCTTGTATCGGGTGC (SEQ ID NO 191)

25 or to equivalents of said probe,
and/or to any probe derived from SEQ ID NO 171, 172 or 173, provided said probe hybridizes specifically to M.
haemophilum.

18. Method according to claim 1 to detect and identify one or more *Mycobacterium malmoense* strains in a sample, wherein step (iii) comprises hybridizing to at least one of the following probes:

30

MML-ICG-1 : CGGATCGATTGAGTGCTTGTCCC (SEQ ID NO 188)

MML-ICG-2 : TCTAAATGAACGCACTGCCGATGG (SEQ ID NO 189)

35

or to equivalents of said probes,
and/or to any probe derived from SEQ ID NO 107 provided said probe hybridizes specifically to M. malmoense.

40 19. Method according to claim 1 to detect and identify one or more Mycobacterium strains in a sample, wherein step
(iii) comprises hybridizing to at least one of the following probes:

MYC-ICG-1 : ACTGGATAGTGGTTGCGAGCATCTA (SEQ ID NO 1)

45 MYC-ICG-22 : CTTCTGAATAGTGGTTGCAGACATCT (SEQ ID NO 2)

or to equivalents of said probes.

50 20. Method according to claim 1 wherein step (iii) is further characterized that the polynucleic acids of step (i) or (ii) are hybridized with a set of probes comprising at least two probes under the same hybridization and wash conditions, with said probes being selected from the sequences of table 1a or equivalents thereof, and/or from taxon-specific probes derived from any of the spacer sequences as represented in figures 1-103, with said taxon-specific probe being selected such that it is capable of hybridizing under the same hybridization and wash conditions as at least one of the probes of table 1a.

55. 21. Method according to claim 20, wherein the sample is originating from the respiratory tract and wherein step (iii) is further characterized that the set of probes comprises at least one probe chosen from the following spacer probes:

5	MYC-ICG-1 :	ACTGGATAGGGTGCAGCATCTA	(SEQ ID NO 1)
	MYC-ICG-22 :	CTTCTGAATAGGGTGCAGCATCT	(SEQ ID NO 2)
10	MTB-ICG-1 :	GGGTGCATGACAACAAAGTTGCCA	(SEQ ID NO 3)
	MTB-ICG-2 :	GACTTGTCCAGGTGTTGTCCCAC	(SEQ ID NO 4)
15	MTB-ICG-3 :	CGGCTAGCGGTGGCGTGTCT	(SEQ ID NO 5)
	MAI-ICG-1 :	CAACAGCAAATGATTGCCAGACACAC	(SEQ ID NO 6)
20	MIL-ICG-11 :	GAGGGGTTCCCGTCTGTAGTG	(SEQ ID NO 7)
	MIL-ICG-22 :	TGAGGGGTTCTCGTCTGTAGTG	(SEQ ID NO 8)
25	MAC-ICG-1 :	CACTCGGTCGATCCGTGTGGA	(SEQ ID NO 9)
	MAV-ICG-1 :	TCGGTCCCGTCCGTGTGGAGTC	(SEQ ID NO 10)
30	MAV-ICG-22 :	GTGGCCGGCGTTATCGAAA	(SEQ ID NO 11)
	MIN-ICG-1 :	GCATAGTCCTTAGGGCTGATGCGTT	(SEQ ID NO 12)
	MIN-ICG-2 :	GCTGATGCGTTCGTCGAAATGTGTA	(SEQ ID NO 13)
35	MIN-ICG-22 :	CTGATGCGTTCGTCGAAATGTGT	(SEQ ID NO 14)
	MIN-ICG-222 :	TGATGCGTTCGTCGAAATGTGT	(SEQ ID NO 15)
	MIN-ICG-2222 :	GGCTGATGCGTTCGTCGAAATGTGTA	(SEQ ID NO 16)
40	MAL-ICG-1 :	ACTAGATGAACCGCGTAGTCCTTGT	(SEQ ID NO 17)
	MHEF-ICG-1 :	TGGACGAAAACC GG GTGCACAA	(SEQ ID NO 18)
	MAH-ICG-1 :	GTGTAATTCTTTAACTCTTGTGTAAAGTAAGTG	(SEQ ID NO 19)
45	MCO-ICG-11 :	TGGCCGGCGTGTTCATCGAAA	(SEQ ID NO 20)

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	MTH-ICG-11 :	GCACTTCAATTGGTGAAGTGCAGGCC	(SEQ ID NO 21)
5	MTH-ICG-2 :	GCGTGGTCTTCATGCCGG	(SEQ ID NO 22)
	MEF-ICG-11 :	ACCGTGGCCTCGTGG	(SEQ ID NO 23)
	MSC-ICG-1 :	TCGGCTCGTCTGAGTGGTGTC	(SEQ ID NO 24)
	MKA-ICG-1 :	GATCGTTCGCTACGGTAGCGT	(SEQ ID NO 25)
10	MKA-ICG-2 :	GATCGTTGCCTACGGTAGCGT	(SEQ ID NO 26)
	MKA-ICG-3 :	ATCGTTGCCCTACGGTAGCGT	(SEQ ID NO 27)
	MKA-ICG-4 :	CGGGCTCTGTTGAGAGTTGTC	(SEQ ID NO 28)
15	MKA-ICG-5 :	CCCTCAGGGATTCTGGGTGTTG	(SEQ ID NO 182)
	MKA-ICG-6 :	GGACTCGTCCAAGAGTGTGTC	(SEQ ID NO 183)
	MKA-ICG-7 :	TCGGGCTTGGCCAGAGCTGTT	(SEQ ID NO 184)
20	MKA-ICG-8 :	GGGTGCGAACAGCAAGCGA	(SEQ ID NO 185)
	MKA-ICG-9 :	GATCGTTGCCCTACGGG	(SEQ ID NO 186)
	MKA-ICG-10 :	CCCTACGGTAGCGTGTCTTTG	(SEQ ID NO 187)
25	MCH-ICG-1 :	GGTGTGGACTTGACTTCTGAATAG	(SEQ ID NO 29)
	MCH-ICG-2 :	CGGCAAAACGTCGGACTGTCA	(SEQ ID NO 30)
	MCH-ICG-3 :	GGTGTGGCCTTGACTTATGGATAG	(SEQ ID NO 210)
30	MGO-ICG-1 :	AACACCCTGGGTGCTGTCC	(SEQ ID NO 31)
	MGO-ICG-2 :	GTATCGTTGTCGTTCGCGGC	(SEQ ID NO 32)
	MGO-ICG-5 :	CGTAGGGGTCATCGTCTGTAG	(SEQ ID NO 33)
35	MUL-ICG-1 :	GGTTCGGGATGTTGTCCCACC	(SEQ ID NO 175)
	MGV-ICG-1 :	CGACTGAGGTCGACGTGGTGT	(SEQ ID NO 176)
	MGV-ICG-2 :	GGTGTGAGCATTGAATAGTGGTTGC	(SEQ ID NO 177)
40	MGV-ICG-3 :	TCGGGCCGCGTGTTCGTAAA	(SEQ ID NO 211)
	MXE-ICG-1 :	GTTGGGCAGCAGGCAGTAACC	(SEQ ID NO 178)
	MSI-ICG-1 :	CCGGCAACGGTTACGTGTT	(SEQ ID NO 179)
45	MFO-ICG-1 :	TCGTTGGATGGCCTCGCACCT	(SEQ ID NO 180)
	MFO-ICG-2 :	ACTTGGCGTGGGATGCGGGAA	(SEQ ID NO 181)
	MML-ICG-1 :	CGGATCGATTGAGTGCTTGTCCC	(SEQ ID NO 188)
50	MML-ICG-2 :	TCTAAATGAACGCAGGCCATGG	(SEQ ID NO 189)
	MCE-ICG-1 :	TGAGGGAGCCCGTGCCTGTA	(SEQ ID NO 190)
	MHP-ICG-1 :	CATGTTGGGCTTGATCGGGTGC	(SEQ ID NO 191)
55	PA-ICG 1 :	TGGTGTGCTGCGTGAATCCGAT	(SEQ ID NO 34)

PA-ICG 2 :	TGAATGTTCGTGGATGAACATTGATT	(SEQ ID NO 35)
PA-ICG 3 :	CACTGGTGATCATTCAAGTCAAG	(SEQ ID NO 36)
5 PA-ICG 4 :	TGAATGTTCGT(G/A)(G/A)ATGAACATTGATTCTGGTC	(SEQ ID NO 37)
10 PA-ICG 5 :	CTCTTCACTGGTGATCATTCAAGTCAAG	(SEQ ID NO 38)
MPN-ICG 1 :	ATCGGTGGTAAATTAAACCAAATCCCTGT	(SEQ ID NO 49)
15 MPN-ICG 2 :	CAGTTCTGAAAGAACATTCCGCTTCTTC	(SEQ ID NO 50)
MGE-ICG 1 :	CACCCATTAATTTTCGGTGTAAAACCC	(SEQ ID NO 51)
Mycoplasma-ICG :	CAAAACTGAAAACGACAATCTTCTAGTTCC	(SEQ ID NO 52)
20 STAU-ICG 1 :	TACCAAGCAAAACCGAGTGAATAAAGAGTT	(SEQ ID NO 53)
STAU-ICG 2 :	CAGAAGATGCGGAATAACGTGAC	(SEQ ID NO 54)
STAU-ICG 3 :	AACGAAGCCGTATGTGAGCATTGAC	(SEQ ID NO 55)
STAU-ICG 4 :	GAACGTAACCATGTTAACGTTGACTTAT	(SEQ ID NO 56)
25 ACI-ICG 1 :	GCTTAAGTGCACAGTGCTCTAAACTGA	(SEQ ID NO 57)
ACI-ICG 2 :	CACGGTAATTAGTGTGATCTGACGAAG	(SEQ ID NO 58)

30 or equivalents of said probes,
and/or wherein the set of probes comprises at least one taxon-specific probe derived from the spacer region sequence corresponding to one of the micro-organisms to be detected in said sample, said spacer region sequence being chosen from any of the sequences as represented by SEQ ID NO 76 to 106, 157 to 174, 124, 125, 111 to 115, 139 to 144, or 126 to 130,
35 and with said probes or equivalents being possibly used in combination with any probe detecting at least one of the following organisms: Haemophilus influenzae, Streptococcus pneumoniae, Moraxella catarrhalis or Bordetella pertussis.

22. Method according to claim 20, wherein the sample is taken from the cerebrospinal fluid, and wherein step (iii) is further characterized that the set of probes comprises at least one probe chosen from the following spacer probes:

40 MYC-ICG-1 :	ACTGGATAGTGGTTGCGAGCATCTA	(SEQ ID NO 1)
MYC-ICG-22 :	CTTCTGAATAGTGGTTGCGAGCATCT	(SEQ ID NO 2)
45 MTB-ICG-1 :	GGGTGCATGACAACAAAGTTGGCCA	(SEQ ID NO 3)
MTB-ICG-2 :	GACTTGTCCAGGTGTTGTCCCAC	(SEQ ID NO 4)
50 MTB-ICG-3 :	CGGCTAGCGGTGGCGTGTCT	(SEQ ID NO 5)
LIS-ICG 1 :	CAAGTAACCGAGAATCATCTGAAAGTGAATC	(SEQ ID NO 39)

LMO-ICG 1 : AAACAAACCTTACTTCGTAGAAGTAAATTGGTTAAG (SEQ ID NO 40)

5 LMO-ICG 2 : TGAGAGGTTAGTACTTCTCAGTATGTTGTT (SEQ ID NO 41)

LMO-ICG 3 : AGGCACATGCTGAAGCATCGC (SEQ ID NO 42)

10 LISP-ICG 1: CGTTTCATAAGCGATCGCACGTT (SEQ ID NO 212)

or equivalents of said probes,
and/or wherein the set of probes comprises at least one taxon-specific probe derived from the spacer region sequence corresponding to one of the micro-organisms to be detected in said sample, said spacer region sequence being chosen from any of the sequences as represented by SEQ ID NO 116, 117, 118-121, or 213-215,
15 and with said probes or equivalents being possibly used in combination with any probe detecting at least one of the following organisms: Neisseria meningitidis, Haemophilus influenzae or Streptococcus pneumoniae.

23. Method according to claim 1, to detect and identify specifically Mycobacterium species in a sample, wherein step
20 (ii) comprises amplification of the 16S-23S rRNA spacer region or a part of it, using at least one of the following primers:

MYC-P1: TCCCTTGTGGCCTGTGTG (SEQ ID NO 65)
25 MYC-P2: TCCTTCATCGGCTCTCGA (SEQ ID NO 66)
MYC-P3: GATGCCAAGGCATCCACC (SEQ ID NO 67)
MYC-P4: CCTCCCACGTCCCTTCATCG (SEQ ID NO 68)
30 MYC-P5: CCTGGGTTTGACATGCACAG (SEQ ID NO 192)

or equivalents of these primers, said equivalents differing in sequence from the above mentioned primers by changing one or more nucleotides, provided that said equivalents still amplify specifically the spacer region or part of it
35 of Mycobacterium species.

24. Composition comprising at least one of the probes or primers as defined in claims 1 to 19 and 23.

25. Probe as defined in any of claims 1 to 19.

40 26. Primer as defined in claim 23.

27. Reverse hybridization method according to any of claims 1 to 23 wherein the probes are immobilized on a known location on a solid support, more preferably on a membrane strip.

45 28. Kit for the detection and identification of at least one strain of Mycobacterium species, or for the simultaneous detection and identification of several micro-organisms of which at least one strain of Mycobacterium species in a sample, comprising the following components:

50 (i) when appropriate, at least one suitable primer pair to allow amplification of the 16S-23S rRNA spacer region, or a part of it;
(ii) at least one of the probes as defined in claim 25;
(iii) a buffer, or components necessary to produce the buffer, enabling a hybridization reaction between said probes and the polynucleic acids present in the sample, or the amplified products thereof;
55 (iv) a solution, or components necessary for producing the solution, enabling washing of the hybrids formed under the appropriate wash conditions;
(v) when appropriate, a means for detecting the hybrids resulting from the preceding hybridization.

Figure 1

AAGGAGCACC ACGAAAACGC CCCAACTGGT GGGCGTAGG CCGTGAGGGG TTCTTGTCTG TAGTGGCGA
GAGCCGGGTG CATGACAACA AAGTTGGCA CCAAACACACT GTGGGTCTT GAGGCAACAC TCGGACTTGT
TCCAGGTGTT GTCCCACCGC CTTGGTGGTG GGGTGTGGTG TTTGAGAACT GGATAGTGGT TGCGGAGCATC
AATGGATAAG CTGCCGGCTA GCGGTGGCGT GTTCTTGTG CAATATTCTT TGTTTTTGT TTGTGT

(SEQ ID NO 76)

Figure 2

AAGGAGCACC ACCAAAAGCA CCCCAACTGG TGGGGTGGCA GCCGTGAGGG GTTCGGCGTCT GTAGTGGACG
GGGGCCGGNT GCGCAACAGC AAATGATTGC CAGACACACT ATTGGGGCCT GAGACAAACAC TCGGGTCCGTC
CGTGTGGACT CCCTCCATCT TGGTGGTGG GTGTGGTGT TGAGTATTGG ATAGTGGTTG CGAGGCATCTA
GATGAGCGCA TGGTCTTCGT GGCGGGCGTT CATCGAAATG TGTAAATTCT TCCTTAACTC TTGTGTGT

(SEQ ID NO 77)

Figure 3

AAGGAGCACC ACCAAAAGCA CCCCAAATCGG TGGGGTGCAGA GCCGGTGAGGG GTTCCCGTCT GTAGGTGGACG
GGGGCCGGGT GCGCAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGTCCGTC
CGTGTGGAGT CCCTCCATCT TGTTGGTGGG GTGTGGTGT TGAGTATGG ATAGTGGTTG CGAGGATCTA
GATGAGGCCA TGGTCTTCGT GGCGGGCGGT CATCGAAATG TGTAAATTCT TTGTTAACTC TTGTTGTGT

(SEQ ID NO 78)

Figure 4

AAGGAGCACC ACCAAAAGCA CTCCAAATTGG TGCGGTGCCGA GCCGCTGAGGG GTTCCCGTCT GTAGTGGACG
GGGGCCGGNT GCACAACAGC AAATGATTGC CAGACACACT ATGGGGCCCT GAGACAACAC TCGGTGATC
CGTGTGGAGT CCCTCCATCT TGTTGGTGG TGACTATTGG ATAAGTGGTTG CGAGGCATCTA
GATGAGCGCA TAGTCCTTGT GGCTGATGCG CTCGTCGAAA TGTGTAATTI CTTCCTTGGT GTNTGTGTGT
(SEQ ID NO 79)

Figure 5

AAGGAGCACC ACGAAAGCA TCCCAATTGG TGGGGTGCAGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG
AAAACGGGT GCACAAACAGC AAATGATTGC CAGACACACT ATGGGCCCT GAGACAACAC TCGGGTCGATC
CGTGTGGAGT CCCTCCATCT TGTTGGGG GTGTGGTGTG TGAGTATTGG ATAGTGGTTG CGAGCATCTA
GATGAGGGG TAGTCCCTTG TGGCTGATGC GTTCATCAA ATGTGTAATT TCTTTTGG TTNTNTGTGTG
T

(SEQ ID NO 80)

Figure 6

AAGGAGGCC ACCGAAAGCA CTCCCAATTGG TGCGGTGCGA GCCGTTGACGG GTTTCCCGTCT GTAGTGGACG
GGGGCCGGGT GCACAACAGC AAATGATATGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGGTCGATC
CGTGTGGAGT CCCTCCATCT TGTTGGTGGG GTGTTGGTGG ATAGTGGTTG CGAGGCATCTA
GATGAGGCCA TAGCCCTTGC GGCTGATGGC TTTCGNCGAAA TTGTTAAATT CTTCCTCTGGT TTCTGTGTGT

(SEQ ID NO 81)

Figure 7

AAGGAGGCC ACCAAAAGCA CTCCTAAATTGG TCGGGTGGCGA GCCGGTGAGGG GTTCTCGTCT GTAGTGGACG
GNAAGCCGGGT GCACAAACAGC AAATGATGTC CAGACACACT ATTGGGGCCCT GAGACACACAC TCGGGTGCATC
CGTGTGGAGT CCCTCCCATCT TGTTGGTGGG GTGTGGTGT TGAGTATTTGG ATAGTGGTTG CGAGGCATCTA
GATGAGCCCG TAGTCCTTCG TGGCTGATGC GTTCATCGAA ATGTGTATT TCTTCTTGG TTTTGGGTGT
GT

(SEQ ID NO 82)

Figure 8

AAGGAGGCC ACC ACGAAAAGCA CTC CAAT TGG TGG GGT GCG GA GCC GGT GAG GG GT TAGT GG GAC G
GGG CCG GGT GCACA ACAGC AAAT GAT CGC CAGA CAAC ACT ATT GGG CCCT T GAG CAAC AC TCG GT CG GAT C
CGT GT GG AGT CC CT CC ATCT TGG TGG GT GG GT GG TT TG AGT AT TGG AT AGT GG TT GG AT AGC AT CTA
GAT GAG GGCA TAG TC CT TTG GGG CT GAT GT GT AAT GT GT TAAT TT CT TT TT NG GT TT TT NG GT TT
GT

(SEQ ID NO 83)

Figure 9

AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGTGCGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG
GGAGCCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGGGCCT GAGACAAACAC TCGGGTCGATC
CGTGTGGAGT CCCTCCATCT TGTTGGTGG GTGTGGTGT TGAGTATTGG ATAGTGGTTG CGAGCATTCA
GATGAGCGCG TAGTCCTTCG TGGCTGATGC GTTCATTGAA ATGTGTAATT TCTTCTCTGG TTTTTGTGTG
T

(SEQ ID NO 84)

Figure 10

AAGGAGGCC ACCAAAAGCA CTCCTAAATTGG TGGGGTGGGA GCGGTGAGGG GTTCCCGTCT GTAGTGGACCG
GGGGCCGGGT GCACAACAGC AAATGATTTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGGTCGATC
CGTGTGGAGT CCCTCCATCT TGTTGGGG GTGTGGTGT TGAGTATTGG ATAGTGGTTG CGAGGCATCTA
GATGAGGCCA TAGTCCTTGT GGCTGATGGC CTCTGTGAA TGTTGAATT CTTCCTTGGT TTTCCTGTGT

(SEQ ID NO 85)

Figure 11

AAGGAGCACC ACGAAAGCA CTCCAATTGG TGGGTGCGA GCCGTGAGGG GTTCCCGTCT GTAGTGGACG
GGGGCCGGGT GCGCAACAGC AAATGATTGC CAGACACACT ATTGGCCCT GAGACACAC TCGGTGCGATC
CGTGTGGAGT CCCTCCATCT TGGTGGTGG GTGTTGGTGT TTGAGTATTG GATACTGGTT GCGAGCATCT
AGATGACGCC GTAGTCCTTG TGGCTGATGC GTTCGTCGAA ATGTGTAAATT TCTTCTTGG GTTTTGTGT
GT

(SEQ ID NO 86)

Figure 12

AAGGAGGCC ACCGAAAGCA CCCCAAATGG TGGGGTGCAGA GCCGGTGAGGG GTTCTCGTCT GTAGTGGACG
GNAGCCGGNT GCGCAACAGC AAATGATG CAGACACACT ATGGGCCCT GAGACAACAC TCGGNCGATC
CGTGTGGAGT CCCTCCATCT TGTTGGGG GTGTNGTGG TGAGTATTGG ATAGTGGTTG CGAGCATCTA
GATGGGGCG TAGTCCTTG TGACTGATGC GTTCATCAA ATGTGTAATT TCTTTTTGN NTTTNGTGTG
T

(SEQ ID NO 87)

Figure 13

AAGGAGCACC ACGAAAGCA CTCCAATTGG TGGGTGCGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG
GGAACCGGGT GCACAAACAGC AAATGATTGC CAGACACACT ATTGGCCCT GAGACAACAC TCGGGTCGATC
CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTTGGTGTT TGAGTATGG ATAGTGGTTG CGAGCATCTA
GATGAGGGCA TAGTCCTTGG TGGCTGACGC GTTCATCGAA ATGTGTAATT TCTTCCTTGG TTTTGTGTG
T

(SEQ ID NO 88)

Figure 14

AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCAGA GCCGGTGANGG GTTCGGGTCT GTAGTGGACG
GGGGCCGGGT GCACAAACAGC AAATGATATGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGTGATC
CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT TGAGTATGG ATAGTGGTTG CGAGCATCTA
GATGAGGGCA TAGCCTTAG GGCTGATGCG TTGTCGNAA TGTGTAATT TGTTGTGTGT TTCTCTTGGT

(SEQ ID NO 89)

Figure 15

AAGGAGGCACC ACGAAAAGCA TCCCAATTGG TGGGGTGCAGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG
AAAACGGGT GCACAAACAGC AAATAATTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGGTCGATC
CGTGTGGTGT CCCTCCATCT TGTTGGTGGG GTGTGGTGT TGAGTATTGG ATAGTGGTTG CGAGCATCTA
GATGAAACGGG TAGTCCCTCG TGGCTGACGT GTTCATCGAA ATGTGTAATT TCTTNTNTA ACTCTTGTGT
GT

(SEQ ID NO 90)

Figure 16

AAGGAGCACC ACGAAAAGCA CCCCAATTGG TGGGGTGGGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG
GGAGCCGGGT GCACAACAGC AAATGATGCC CAGACACACT ATGGGCCCT GAGACAACAC TCGGTCAAGTC
CGTGTGGTGT CCCTCCATCT TGTTGGTGGG GTGTGGTGT TGAGTATTGG ATAGTGGTTG CGAGGCATCTA
GATGAAACGCG TAGTCCCTGT GACTGACGTG TTCAATCGAAA TTCAATCGAAA TTCAATCGAAA TTCAATCGAAA

(SEQ ID NO 91)

Figure 17

AAGGAGGCC ACCAAAGCA CTTCAATTGG TGAAGTGGCA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG
AAAGCCGGGT GCACAACAGC AAATGATTGC CAGACACACT ATTGGCCCT GAGACAAACAC TCGGTCCAAC
CGTGTGGAGT CCCTCCATCT TGTTGGTGGG GTGTGGTGT TGAGTATTGG ATAGTGGTTG CGAGCATCTA
GATGAAACGGG TGGTCTTCAT GGCCGGGTG TTCATCGAAA TGTGTAATA TCTCTCTGGT TTTCGGTGTG
T

(SEQ ID NO 92)

Figure 18

AAGGAGGCC ACCAAAAGCA CTTCAATTGG TGAAGTGCAGA GCGGTGAGGG GTTCTCGTCT GTAGTGGACG
AAAACCGGNT GCACAACAGC AAATGATGCA CAGACACACT ATTGGGCCT GAGACAACAC TCGGTGGATC
CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGGTGGTGG TGAGTATGG ATAGTGGTTG CGAGCATCTA
GATGAAACGGG TGGTCTTCAT GCCCCGGCGTG TTCAATCGAAA TGTGTAATT CTTTTNAC TCTTGTGTGT

(SEQ ID NO 93)

Figure 19

AAGGAGCACC ACGAAAGCA CTTCAATTGG TGAAGTGCAGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG
AAAGCCGGGT GCACAAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGGTCAAAC
CGTGTGGAGT CCCTCCATCT TGGTGGTGGG GTGTGGTGT TGAGTATGG ATAGTGGTTG CGAGCATCTA
GATGAACGCG TGGTCTTCAT GGCGGGGTG TTCATCGAAA TGTGTAATT TTCTTGGT TTTNGTGTGT

(SEQ ID NO 94)

Figure 20

AAGGAGGCC ACCGAAAGCA CTTCAATTGG TGAAGTGCAGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG
AAAACCGGGT GCACAAACAGC AAATGATTC CAGACACACT ATGGGCCCT GAGACAACAC TCGGTGATC
CGTGTGGAGT CCCTCCATCT TGTTGGGG GTGTGGTGT TGAGTATTGG ATAGTGGTT CGAGCATCTA
GATGAACGGG TAGTCCTCG NGGNNCNGCGT GTTCATCGAA ATGTGTAATT TCTNTNTAA CTCTNGTGTG
T

(SEQ ID NO 95)

Figure 21

AAGGAGCACC ACGAAAAGCA TCCCATAATGG TGGGGTGTGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG
AAAACCGGGT GCACAAACAGC AAATGATTC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGTGGATC
CGTGTGGAGT CCCTCCCATCT TGGTGGTGGG GTGTGGTGT TGAGTATTGG ATAGTGGTTG CGAGGCATCTA
GATGAACGCG TAGTCCTTCG GGGCCGGCGT GTTCATCGAA ATGTGTAAATT TCTTTTAA CTCTTGTTG
T

(SEO ID NO 96)

Figure 22

AAGGAGGCC ACCAAAAGCA CTTCANTTGG TGAAGTGGCGA GCCGTGAGGG GTTCCTCGTCT GTAGTGGACG
AAAACGGGT GCACAAACAGC AAATGATGG CAGACACACT ATTGGGCCT GAGACAACAC TCGGTGAAAC
CGTGTGGAGT CCCCTCCATCT TGGTGGTGG TGAGTATTGG ATAGTGGTGG CGAGGCATCTA
GATGAAACGGG TGGTCTTCAAT GGCGGGCGTG TTCAATCGAAA TGTTGAATT CTTCCTTAAC TCTTGTGTGT

(SEQ ID NO 97)

Figure 23

AAGGAGGCC ACC ACGAAAGCA CTTCAATTGG TGAAGTGGCA GCCGTGAGGG GTTCTCGTCT GTAGTGACG
AAAACGGGT GCACAAACAGN AAATGATTC CAGACACACT ATTGGCCCT GAGACAACAC TCGGTGGATC
CGTGTGGAGT CCCTCCATCT TGGTGGTGG GTGTGGTGT TGAGTATGG ATAGTGGTTG CGAGCATCTA
GATGAACGGG TGGTCTTCAT GGCCNGGGTG TTCATCGAA TGTGTAATT CTTTTAAC TCTTGTGTGT

(SEQ ID NO 98)

Figure 24

AAGGAGGCACC ACGAAAAGCA CTTCAATTGG TGAAGTGCCA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG
AAAACGGGGT GCACAAACAGC AAATGATTGC CAGCACACT ATGGGGCCCT GAGACAACAC TCGGGTCGATC
CGTGTGGAGT CCCTCCATCT TGGTGGTGG GTGTGGTGT TGAGTATTGG ATAGTGGTGT CGAGCATCTA
GATGAAACGGG TGGTCTTCAT GGCGGGCGTG TTCATCGAAA TGTGTAATT CTTTTTAAC TCTTGTGTGT

(SEQ ID NO 99)

Figure 25

AAGGAGCACC ACCAAAGCA CCCCAACTGG TGGGGTGCAGA GCGCGTAGGGG GTCCCTCGCCCT GTAGTGGGGCG
GGGGCGGGGT GCAACAACAGC AAATGATTGC CAGACACACT ATTGGGCCCT GAGGCAACAC TCGGCTTCGTT
CTGAGTGGTG TCCCTCCATC TTGGTGGTGG GGTGTGGTGT TTGAGTATTG GATAAGTGGTT GCGAGCACT
AACGGATGC GTGGCCGGCA ACGGTGGCGT GTTCGTTGAA ATGTGTATT TCTTTTGTGTG T
(SEQ ID NO 100)

Figure 26

AAGGAGCACC ACCAAAAGCA TCCCAACAAG TGGGGTGC_{AA} NCCGTGAGGG GTTCTCGTCT GTAGTGGACG
AAAGCCGGGT GCACGACAAAC AAGCAAAGCC AGACACACTA TTGGGTCCCTG AGGCAACACT CGGGCTCTGT
TCGAGAGTGT TCCCACCATC TTGGTGGTTG GGTGTGGTGT TTGAGAATG GATA GTGGTTT GGAGGCATCA
AATGGATGCG TTGCCCTACG GGTAGCGGTGT TCTTTTGTGC AATTATTC TTTGGTTTT GTGT

(SEQ ID NO 101)

Figure 27

AAGGAGCACC ATTCCCCAGT CGATGAACATA GGGAACATAA AGTAGGCATC TGTAGTGGAT ATCTACTTGG
TGAATATGTT TGTAAATCC TGTCACCCCC GTGGATGGGT AGTCGGAAA ACGTCGGACT GTCATAAGAA
TTGAAACGGCT GGCAACACTGT TGGGTCCGTGA GGCAACACGT TGTGTTGTCA CCCTGCTTGG TGGTGGGGTG
TGGACTTTGA CTTCTGAATA GTGGTTGCCA GCATCTAAC ATAGCCTCGC TCGTTTTCGA GTGGGGCTGG
TTTTGCAATT TTA

(SEQ ID NO 102)

Figure 28

AACGGACC ATTCCCGACT CGGATGAAC T AGGAAACATA AAGTAGGCAT CTGTAGTGGG TATCTACTTG
GTGAATATGT TTTGTAATC CTGTCCACCC CCGTGGATGG GTAGTCGGCA AAACGTCGGA CTGTCATAAG
AATTGAAACG CTGGCACACT GTTGGGTCT GAGGCAAACAC GTTGTGTTGT CACCCCTGCTT GGTGGTGGGG
TGTGGACTTT GACTTCTGAA TACTGGTTGC GACCATCTAA ACATAGCCCTC GCTCGTTTC GAGTGAGGCT
GGTTTTGCA ATTATA

(SEQ ID NO 103)

Figure 29

AAGGAGCACC ACGAAGAGCA CTCCAATTGG TGGGGTGCAG GCGGTGAGGG GTCATCGTCT GTAGTGGACG
AAGACCCGGGT GCACGGACAAAC AAGCTAACCC AGACACACTA TTGGGGTCCCTG AGGCAACACC CTCGGGTGCT
GTCCCCCCAT CTGGTGGTG GGGTGGTG TTGAGAATT GGATAGTGGT TGCGAGGCATC AAAATGTATG
CGTTGTCGTT CTGGGCAACG TTGTTCTTTT GTGCAATTAA TTCTTTGGTT TTGTAGTGT TTGT

(SEQ ID NO 104)

Figure 30

AAGGAGCACC ACGAAGAGCA CTCCAATTGG TGCGGTGCGA GCCGNGAGGG GTCATCGTCT GTAGTGGACG
AAGACTGGGT GCACGACAAC AAAGCAAGCC AGACACACTA TTGGGTCCCTG AGGCAACACC CTCGGGTGCT
GCCCTCCAT CTTGGTGGTG GGGTGGTG TTTGAGAACT GGATAAGTGGT TGCGAGGCATC AAAAATGTAT
GCGTTGTGCT TCGCGACAACT GTGTTCTTT TGTGCAATT TAATTCTTT GGTGTTGGTA GTGTTTGT

(SEQ ID NO 105)

Figure 31

AAGGAGCACC ACCGAGAAGCA CTCCAATTGG TGGGGTGC_{AA} GCCGTGACGG GTCATCGTCT GTAGTGGACG
AAGACCCGGGT GCACGACAAAC AGGCAAAGCC AGACACACTA TTGGGTCC_{TA} AGGCAACACC CTCGGGGTGGCT
GTCCCCCAT CTGGTGGTG GGGTGTGGTG TTGAGAACT GGATAGTGGT TCGGAGGCATC AAAATGTATG
CGTTGTCGTT CGGGCAACG TGTTCTTTT GTGCAATT TATTCTTTGG TTGTTGTAGT GTTTGT

(SEQ ID NO 106)

Figure 32

AAGGAGGCACC ACGAAAAGCA CCCCAATTGG TGGGGTGC_{AA} GCGGTGAGGG GTAGTGGGG
GGGCCGGGTG CGCAACAGCA ATGATGCC AGACACACTA TTGGGCCCTG AGGCAAACACT CGGATCGATT
GAGTGCTTGT CCCCCCATCT TGCTGGTGG GTGTGGTGT TGAGAACCTGG ATAGTGGTTG CGAGCATTCA
AATGAACGCA CTGCCGATGG TGGTGTGTC GTTTTGTA ATTATATCT TTGGTTTTG TGTGTTG

(SEQ ID NO 107)

Figure 33

AAGGAGGCACC ACGAAAAGCA C'TCCAATTGG TGGGGTGGCA GCCGTNAGGG GTTCTCGTCT GTAGTGGATG
GCCAGCCGGGT GCACANCAGC AAATGATTGC CAGACACACT ATTGGGCCCT GAGACAAACAC TCGGTCACTC
CGTGTGGAGT CCCTCCATCT TGTTGGTGGG GTGTGGNGTT TGAGTATTGG ATAGTGGTTG CGANCATCTA
GATGAACGGG TAGTCCTCNG TGGCTGACGT GTTCATCAA ATGTGTAATT TCCTTTANGG GTTNGGTGT
CT

(SEQ ID NO 108)

Figure 34

AAGGAGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCAGA GCCGNGAGGG GTTCTCGCCT GTAGTGGNCG
AGGGCCGGAT GCACAAACA ACATGATTGC CAGACACACT ATTGGGCCT GANACAAAC TCGGCCAGTC
CGTGTGGTGT CCCTCCATCT TGGTGGTGG GTGTGGTGT TGAGTATNGG ATAGTNGTGA TAGTNGTGA NGANCATCTA
AACGGTGCCT TNGNCNNGA CGGTGGCGTG TTCGNTAAAA TGTGTAATT CTTTTNNNGT TTGGGTGTNT

(SEQ ID NO 109)

Figure 35

AAGGAGGCACC ACGAAAAGCA CTCCAATTGG TGGGGTGCAGA GCCGGTGACGG GTTCTCGCCCT GTAGTGGGG
ANGGCCGGGT GCACAAACAC AAATGATTGC CAGACACACT ATGGGCCCT GAGACAAACAC TCGGCCAGTC
CGTGTGGTGT CCNCATCT TGTTGGTGG GTAGTATGG ATAGTGGTTG CGAGGCATCTA
AANGGNTGCG TTGCCGNAN CNGTGGCGTN TTGCTTAANTT TTGCTTNGGT TTGTGTGTGT

(SEQ ID NO 110)

Figure 36

ATCGAAGATC CCGGCTTCTT CATAAGCTCC CACAGGAATT GCTTGATTCA CTGGTAGAC GATTGGGTCT
GTAGCCTCAGT TGGTTAGGC GCACCCCTGA TAAGGGTGAAG GTCCGCAGTT CGAACATCTGCC CAGACCCACC
AATTGGTGGT GTGCTGGGT ATCCGATAACG GGGCCATAGC TCAAGCTGGGA GAGGCCCTGC TTTGCACGCC
GGAGGTCAGG AGTTGATCC TCCTTGCTC CACCATCTAA AACAAATCGTC GAAAGCTCAG AAATGAAATGT
TCGTGGATGA ACATTGATT CTGGTCTTTG CACCAACT GTTCTTTAAA AATTGGGTAA AATTCGGTA TGTGATAGAA
GTAAGACTGA ATGATCTCTT TCACTGGTGA TCATTCAAGT CAAGGTTAAA TTTGCCAGTT CAAGGCCGAA
TTTTCGGCGA ATGTGCTCTT CACAGTATAA CCAGATTGCT TGGGGTTATA T

(SEQ ID NO 111)

Figure 37

ATCGAAGACA TCAGCTTCCTT CATAAGTATC CACACGAATT GCTTGATTCA TAGTCGAACG AATGCTGTAA
CGCGACCCGT GTTATAAGGTC TGTTAGCTCAG TTGGTTAGAG CGCACCCCTG ATAAGGGTGA GGTGGGGCACT
TCAAATCTGC CCAGACCTAC CAATTGCTTG GTCGAGAAGA ATACGGGGCC ATAGCTCAGC TGGGAGGCC
CCTGCGCTTGC ACGCAGGAGG TCAGCGGGTTC GATCCCGCTT GGCTCCACCA CTCTCTCGTG TTGGGGTGAG
TGTAAAGAG TTCAGAAATG ATGCCGCTTC AGGTTTGTCC TGGTTGAGTGC TGATTTCCTGG TCTTTTGACC
GGTACGAAAA TCGTTCTTA AAAAATTGGAA TATGTGATAG AAGTGACTGA TTAATTGCTT TCACTGGCAA
TTGATCTGGT CAAGGTAAAA TTGTTAGTTC TCAAAGACCCA AATTTTCGGC GAATGTCCGTC TTCACCGATTG
AGACAGTAAC CAGATTGCTT GGGTTATAT

(SEQ ID NO 112)

Figure 38

ATCGAAGACA CCGGCTTCGT CATAAGCTCC CACACGAATT GCTTGATTCA CTTGGAAAG GCCGATTGGGT
TTAGACCCGA GAGTAACGAT TGGGTCTGTA GCTCAGTGG TTAGAGCGA CCCCTGATAA GGCTGAGGTC
GGCAGTTCGA ATCTGCCAG ACCCACCAAT CGAAAGGGCC ATAGCTCAGC TGGGAGAGCG CCTGCTTTC
ACGCAGGAGG TCAGGGTTC GATCCCCCTT GGCTCCACCA TTAACTCTAG TCCGGAAAG CTCAGAAATG
AGTGTTCACC AGGATGAGGT TGATTGCCCTG GGTTGAACAT TGATTCTGG ACTTTGGGCC AGAAACTGTT
TTAAAAATT TGGGTATGT ATAGAAGTAG ACCGATGTTG ACCGATTTCACT GGCAAGCATGT CGCGTCAAGG
TAAAATTGCC GTGTTCTCTA TGCAAATT CGGCGAATGT CGTCTTCACG TTATAGACAG TAACCAGATT
GCTTGGGGTT ATAT

(SEQ ID NO 113)

Figure 39

ATCGAAGACT TCAGCTTCTT CATAAGTTCC CACACGAATT GCTTGATTCA CTGCGAAA GCGGATTGGGT
TGAGACCGA GAGTGACGAT TGGGTCTGTA GCTCAGTTGG TTAGAGCGCA CCCCTGATAA GGGTGAGGTC
GGCAGTTCGA ATCTGCCAG ACCCACCAT TGTGGGATG GCCAGTGTCA AATGGGGCCA TAGCTCAGCT
GGGAGAGGCGC CTGCTTTGCA CGCAGGAGGT CAGGAGTTGG ATCCTCCTTG GCTCCACCAT CAACTCACGA
TCGCTGAAG CTCAGAAATG AACATGGTA GTTCAATGTT GATTTCCTGGT CTTTGGCCA GAACTGTTCT
TTAAAATTG GGCTATGTA TAGAAGTGAC TAACAGGGTG TTTCACTGCA CGTTGTTAAT CAAGGCAAAA
TTTGGGAGTT CAAGGGCGAA TTTTCGGCGA ATGTCGTCTT CACGTTACGA ATCTATAACC AGATTGCTTG
GGGTTATAT

(SEQ ID NO 114)

Figure 40

ATCGACGACA TCAGCTGTCT CATAAGCTCC CACACGAATT GCTTGATTCA TTGAAGAAGA CGATTAGGTT
AGCAACCTTC GATTGGGTCT GTAGCTCAGT TGGTTAGAGC GCACCCCTGA TAAGGGTGA GTCGGGCAGTT
CGAAATCTGCC CAGACCCACC AATTGCTGG GGCCATAGCT CAGCTGGGAG AGCCGCTGCC TTGCACGGCAG
GAGGTCAAGG GTTGGATCCC GCTTGGCTCC ACCACCCCG ACCACCCCGC TTGCCAGTT GTCAAAGCTT AGAAATGAAAT
ATTGGCGTCC AATATTGATT TCTGAACATT ATCAGAACATCG TTCTTTAAAA ATTGGGTAT GTGATAGAAA
GATAGACTGG ACAGGCACTT CACTGGTGTG TGTTCAGGCT AAGGTAATAAT TTGTGAGTAA TTACAAGTT
TCGGCGAATG TTGTCTTCAAC AGTATAACCA GATTGCTTGG GGTTATAT

(SEQ ID NO 115)

Figure 41

TAAGGAAAAG GAAACCTGTG AGTTTCGTT CTTCTCTGTT TGAGAGGTTA ATTCTTCTCT
ATTAATGTTTG TTCTTTGAAA ACTAGATAAG AAAGTTAGTA AAGTTAGCAT AAATAGGTA AAATTTATGA
CACAAAGTAAC CGAGAACATC ATCGAAAGTGA ATCTTTCATC TGATTGGAAAG TATCATGCT GATAACGAAAA
ATCAGAAAAA CAACCTTAC TTCAATCGAAG TAAATT

(SEQ ID NO 116)

Figure 42

CTAAGGAAAA GGAAACCTGT GAGTTTCGT TCTTCTAT TTGTTCAAGTT TTGAGAGGTT AGTACTTCTC
AGTATGTTG TTCTTTGAAA ACTAGATAAG AAAGTTAGTA AAGTTAGCAT AGATAATTAA TTATTATGA
CACAAAGTAAC CGAGAACATCT CTCAAAGTGA ATCTTTCATC TGATTGGAAG TATCATCGCT GATAACGGAAA
ATCAGAAAAA CAACCTTAC TTCGTAGAAG TAAATT

(SEQ ID NO 117)

Figure 43

TAAGGAAAAG GAAACCTGTG AGTTTCGTT CTTCAGTGT TGAGGGTT TGAGGGTTA TTACTTCCTCT
GTATGTTGT TCTTTGAAAA CTAGATAAGA AAGTTAGTAA AGTTAGCAAA AGTAGTGTAA CTATTTATGA
CACAAGTAAC CGAGAACATCT ATGAAAGTGA ATCTTTCATC TAATTGACG TATCATCGCT GATACAGACA
ATAGAAAAA CAAACCTTAC TTCGACGAAG TAAATT

(SEQ ID NO 118)

Figure 44

GGCCTATAGC TCAGCTGGTT AGAGGCCACG CCTGATAAGC GTGAGGTCGA TGGTTCGAGT CCATTAGGC
CCACTTTTC TTCTGACAG AAGAAACACT GTATAACCTA TTAAAGGGC CTTAGCTAG CTGGAGAGC
GCCTGCTTG CACGCCAGGAG GTCAAGGGTT CGATCCCCT AGGCTCCACC AAAATTGTC TTGAAACT
AGATAAGAAA GTTAGTAAG TTAGCATAAA TAGGTAACCA TTTATGACAC AAGTAACCGA GAATCATCTG
AAAGTGAATC TTTCATCTGA TTGGAAGTAT CATCGCTGAT ACCGAAATC AGAAAAACAA CCTTTACTTC
ATCGAAGTAA ATT

(SEQ ID NO 119)

Figure 45

TAAGGAAAG GAAACCTGTG AGTTTCGTT CTCTCTTATT TGTTCAAGTT TGAGAGGTTA CTCCTTTTA
TGGCAGATAA AGTATGCAAG GCACTATGCT TGAAGCATCG CGCCACTACA TTTTGACGG GCCTATAGCT
CAGCTGGTTA GAGGCCACGC CTGATAAGCG TGAGGTGCGAT GGTTCGAGTC CATTAGGCC CACTTTTCT
TTCTGACATA AGAAATACAA ATAATCATAC CCTTTTACGG GGCCCTTAGCT CAGCTGGAG AGGGCCTGCT
TTGCACGGCAG GAGGTCAAGCG GTTCGATCCC GCTAGGCTCC ACCAAAATG TTCTTGAAA ACTAGATAAG
AAAGTTAGTA AAGTTAGCAT AGATAAATTAA TTATTATGAA CACAAGTAAC CGAGAATCAT CTGAAAGTGA
ATCTTTCATC TGATTGGAAG TATCATCGCT GATACTGGAA ATCAGAAAAA CAACCTTAC TTCGTTAGAAG
TAAATT

(SEQ ID NO 120)

Figure 46

TAGGAAAAG GAAACCTGTN AGTTTNCGTN CTTCTCTGTT TGTNCAGTT TNAGAGGTTA CTCTCTTTNA
TGTCAAGATAA AGTACGGCACG GCACGGTTGCC TTGGGCAAAG AGCCACTACA TTATTGACGG GCCTATAGCT
CAGCTGGTAA GAGCGCACGC CTGATAAAGCG TGAGGTGAT GGTTCGAGTC CATTAGGCC CACTTTCT
TTCTGACAGA AGAAATCATT TGCACATCCT ATTAAATAGG GNCCCTTAGCT CAGCTGGAG AGCGGCCCTGCT
TTGCACGGCAG GAGGTCAAGG GTTCGATCCC GCTAGGCTCC ACCCAAAATT GTTCTTTGAA AACTAGATAA
GAAAGTTAGT AAAGTTAGCA TAAGTAGTAT AACTATTAT GACACAAGTA ACCGAGAATC ATCTGAAAGT
GAATCTTCA TCTAATTGCA CGTATCATCG CTGATACAGA CAATNGAAA AACAAACCTTT ACTTCGACGA
AGTAAATT

(SEQ ID NO 121)

Figure 47

TAAGGATAAG GATAAACTGTC TTAGGGACCGGT TTGACTAGGT TGGCCAAGCG TGTTTTTAAT CTGTGTATTCT
ATTCCTTTTG CATTGTTAAC CGTTTGTTCG AAAACATTAA GTTACCGATC AAGTATGTTA TGTAATAAT
ATGGTAACAA GTAAATTCAAC ATATAATAAT AGACGTTAA GAATATATGT CTTAGGTGA TTGTTAACTTG
CATGGATCAA TAATTTACA

(SEQ ID NO 122)

Figure 48

TAAGGATAAG GAAAGGCCT GAGAAGGTT CTGACTAGGT TGGCAAGCA TTATATGTA AGAGCAAGCA
TTCTATTCA TTGTGTTGT TAAGAGTAGC GTGGTGAGGA CGAGACATAT AGTTTGTGAT CAACTATGTT
ATTGTAAAGA ATAATCATG GTAACAAGTA TATTCACGCC ATAATAATAG ACGTTAACAGA GTATTGCT
TTAGGTGAA GTGCTTGCAT GGATCTATAG AAATTACA

(SEQ ID NO 123)

Figure 49

CAAATGGAGT TTTTATTCTT TATTATCTT AACACCCAT TAATTTC GGTGTTAAA CCCAAATCAA
TGTGTTGGTCT CACAACTAAC ACATTTGGTC AGTTTGATC CAGTTCTGAA AGAATGTTT TGAACAGTTC
TTTCAAAACT GAAAACGACA ATCTTTCTAG TTCCAAAAAT AAATAACAAA GGATCAATAC ATAAGTTAC
TAAGGGCTTA TGTT

(SEQ ID NO 124)

Figure 50

C'TAATGAACT TTTTACTTT TTCTTTCAT CTTTAATAAA GATAAATACT AAACAAAACA TCAAATCCA
TTTATTATTC GGTTGGTAAAT TAAACCCAAA TCCCTGTTC GTCTCACAAAC TAACATATTT GGTCAAGATTG
TATCCAGTTTC TGAAAGAACAA TTTCGGCTTC TTTCAAACT GAAAACGACA ATCTTTCTAG TTCCAAATAA
ATACCAAAAGG ATCAAATACAA TAAGTTACTA AGGGCTTATG GT

(SEQ ID NO 125)

Figure 51

AACGAAAGAT TGACGGATGG TAAGAACCCA CAAACAAGTTG TTCTTCATAG ATGTATCTGA GGGTCTGTAG
CTCAGTTGGT TAGAGCCAC GCCTTGATAAG CGTGGGGTCA CAAGTTCAAG TCTTGTCAAG CCCACCATGA
CTTTGACTGG TTGAAGTTAT AGATAAAAGA TACATGATTG ATGATGTAAAG CTGGGGACTT AGCTTAGTTG
GTAGAGGCC CGCTTTGCAC GCAGGGAGTC AGGAGTTCGA CTCTCCTAGT CTCCACCCAGA ACTTTAAGATA
AGTTCGGATT ACAGAAATTAA GTAAATAAAG ATTGAGATCT TGTTTATTAA ACTTCTGTGA TTTCATTATC
ACGGTAATTAA GTGTGATCTG ACGAAGACAC ATTAACCTCAT TAACAGATTG GCAAAATGAG GCTCTGAATA
AATTGTTCAC TCAAGAGTTT AGGTTAAGCA ATTAAATCTAG ATGAATTGAG AACTAGCAA TAAACTGAAT
CAAGCGTTT GGTATGTGAA TTAGATGTGA AGCTGTACAG TGCTTAAGTG CACAGTGCTC TAAACTGAAA
TGTGAAGTT ACTAACTTGT AGGTAACATC GACTGTTGG GGTGTAT

(SEQ ID NO 126)

Figure 52

AACGAAAGAT TGACGATTGG TAAAGAATCCA CGACAAGTGT TTCTTCATAG ATGTATCTGA GGGTCTGTAG
CTCAGTTGGT TAGAGGCACAC GCTTGATAAG CGTGGGGTCA CAAGTTCAAG TCTTGTCAAG CCCACCATGA
CTTTGACTGG TTGAAGTTAT AGAAAAGAAG ATACATAACT GATGATGTAA GCTGGGGACT TAGCTTAGTT
GGTAGAGCCG CTGCTTTGCA CGCAGGAGGT CAGGAGTTCG ACTCTCCTAG TCTCCACCA

(SEQ ID NO 127)

Figure 53

AACGAAGAT TGATGGCCGG TAAGAATTCCA CAAACAAGTTG TTCTTCGAAG ATGTATCTGA GGGTCTGTAG
CTCAGCTTGGT TAGAGCCACAC GCTTGATAAG CGTTGGGTCA CAAGTTCAAG TCTTGTCAAG CCCACCAAAT
CTGAAAGATA TGTCTGTTCAT TATGATTAAA GCTGGGGACT TAGCTTAGTT GGTAGAGCGC CTGCTTTGCA
CCCAGGAGGT CAGGAGTTCG ACTCTCCCTAG TCTCCACCA

(SEQ ID NO 128)

Figure 54

AACGAAAGAT TGACGATTGG TAAGAATCCA CAACAAGTTG TTCTTCATGA CGATGTATCT GAGGGTCTGT
AGCTCAGTTG GTTAGAGCAC ACGGCTTGATA AGCGTGGGT CACAAGTTCA AGTCTTGTCA GACCCACCAA
ATCTGACTAA CAAGCATTAT TAAATGCTGA ATACAGAAAA ACAGAGACAT TGACTTTATTG ATAAGCTGGG
GACTTAGCTT AGTTGGTAGA GCGCCTGCTT TGCACCGCAGG AGGTCAAGGAG TTCGACTCTC CTAGTCTCCA
CCA

(SEQ ID NO 129)

Figure 55

AACGAAAGAT TGGTGACCGG TAAGAATTCCA CAAACAAGTTG TTCTTCGAAG ATGTATCTGA GGGTCTGTAG
CTCAGTTGGT TAGAGCACAC GCTTGATAAG CGTTGTTCAAG CAAGTTCAAG TCTTGTCAAG CCCACCCTA
CTGACGAAAGT GATGAATAAT CACAAGCTGC TAGATGAAAA GATATGTCGT TCATTATGAT TAAAGCTGGG
GACTTAGCTT AGTTGGTAGA GCGCCCTGCTT TGCACGGAGG AGGTCAAGG TTGCACTCTC CTAGTCTCCA
CCA

(SEQ ID NO 130)

Figure 56

TAAAGGAAGAT CGAGAATTGG AAAGAGGTCG GATTATCCG GATGATCCTT CTCCCATCTTA TTAGAACATA
GATCGCAGGC CAGTCAGCCT GACGATCGCT TGCAGGGGTG CCCCCTTCTGT TTCTCTTCT TCATTGTTGA
TTGCTCACGG GCCGTACGG AGCTGACGCT GCTGGCCCTG CGCAGGGCG GCACCATCAGG GCCGACGGCC
GGTCTGGCCTT GCNAAGCTTC GCTTCGGGGT GGATCTGGGG ATCGGGTAGT AGCGTTTGCG TCGGTATCTG
GGCTTGTAGC TCAGTTGGTT AGAGCACACG CTTGATAAGC GTGGGGTCCG AGGTTCAAGT CCTCCAGGC
CCACCAAGTT ACTTGATGAG GGGCCGTAGC TCAAGCTGGG GAGCACCTGC TTGCAAGGA GGGGTCCGT
GGTTCGATCC CGTCCGGCTC CACCATCATG TTGGTGTGCA GACGGATATT GGCATCAAC AAAAGAAAGA
AACAAAGTTG CGGACTNTTA CGAAAAGTCG CCTGTTCTGT ATGAAATCTG ATGAAATCTG ATGAAATCTG
TCAACTGAAG AGTTGATGTC GCAAGAAAGCT TGCTCAAGCC TTGCATAATG ATGATGTTGTT TTAACCGCCA
TCACCGATG TATCTCGAGA AGCTGGCTT TCTGCTGATA CTGTTGAAAC GAGCATTGC AGTCGAATGG
CAACATTGG CGTGGCATAA TGGGGCTTA AGAGCTGAGT TTGATGGAT ATTGGCAATG AGAGTGATCA
AGTGTCTAA GGGCATTGGT GGATGCCCTG GCATGCAC

(SEQ ID NO 131)

Figure 57

TAAGGAGGAT CGAGAATTGG AAAGAGGCCG GATTATCCG GATGATCCTT CTCATCCTTA TTAGAACATA
GATCGCAGNC CAGTCAGCCT GACGGATCCGT TGCAAGGCCGT CGGCCTTCGT TCTCTTTCT TCATTGTGTA
TTGCTCACGG GCCGTACCGC AGCTGACCGT GCTGGCCCTG CGCAGGGCCG GNCCATCAGG GCCGACGGCC
GGTCGGCCCTT GCGAAGCTTC GCTTCGGGGT GGATCTGTGG ATCGCGTAGT AGCGGTTGGC TCGGTATCTG
GGCTTGTAGC TCAGTTGGTT AGAGCACACG CTGATAAGC GTGGGTCGG AGGTTCAAGT CCTCCCAGGC
CCACCAAGTT ACTTGATGAG GGCCGTAGC TCAGCTGGGA GAGCACCTGC TTGCAAGCA GGGGTCGTC
GGTTCGATCC CGTCCGGCTC CACCATCATG TTGGTGTGA GACGGATATT GCAATCAAAC AAAGAAAGA
AACAAAGTTG CGGACTNTTA CGAAAGCTG CCTGTTCTGT ATGAAATCTGT GAAGAGAAGA TGTAAATCGGA
TCAACTGAAG AGTTGATGTC GCAAGAAGCT TGCTCAAGCC TTGCATAATG ATTGATGTGT TAAACGCCA
TCACCGATTG TATCTCGAGA AGCTGGTCTT TCTGCTGATA CTGTTGAAAC GAGCATTGCA ACTCGAAATGG
CAACATTGG CGTCGCAATAA TGCGGCTTA AGAGCTGAGT TTGATGGAT ATTGGCAATG AGAGTGATCA
AGTGTCTTAA GGGCATTGGT GGATGCCCTG GCATGGCAC

(SEQ ID NO 132)

Figure 58

CCTTAAGAA CTGTTCTTG CAGTGCTCAC ACAGATTGTC TGATGAAGA TAAATAGCAA GGC GTCTTGC
GAAGCAGACT GATA CGTCCC CTT CGTCTAG AGGCCAGGA CACCGCCCT TCACGGCGGT AACAGGGTT
CGAATCCCCCT AGGGGACGCC ACTTGGCGGG TAATGTTGA AAGCGTTGCC ATCAGTATCT CAAA ACTGAC
TTACGAGTCA CGTTTGAGAT ATTGCTT TAAAATCTG GATCAAGCTG AAAATTGAAA CACAGAACAA
CGAAAGTTGT TCGTGAGTCT CTCAAATTG CGAACACACGA TGATGAATCG TAAGAAACAT CTT CGGGTTG
TGA

(SEQ ID NO 133)

Figure 59

CCTTAAAGAA CTGTTCTTGT CAGTGCTCAC ACAGATTGTC TGATGAAAAA CGAGGCAGTAA AACCTCTACA
GGCTTGTAGC TCAAGGTGGTT AGAGGGCACC CCTGATAAGG GTGAGGGTGG TGAGGTCAAGT CCACTCAGGC
CTACCAAATT TTCCCTGAAT ACTGGGTGT GAAATAACTC ACATAACTGAT GTATGCTTCG TTATTCACG
CCTTGTCTCA GGAAAATTAA TCGGTAAMAGA GGTTCTGACT ACACGATGGG GCTATAGCTC AGCTGGGAGA
GGGCCTGCTT TGCACGCCAGG AGGTCTGGG TTGATCCCG CATACTCCA CCATATCGTG ACTGTTACG
AAAAAAATACT TCAGAGTCTA CCTGAAAGGG TTCACTGCCA AGTTTTGCTC TTAAAAAATC TGGATCAAGC
TGAAAATTGA AACACAGAAC AACGAAAGTT GTTCGTGAGT CTCTCAAATT TTGGCAACAC GATGATGAAT
CGTAAGAAC ATCTTCGGGT TTGTA

(SEQ ID NO 134)

Figure 60

CCTTAAGAA GCGTACTTG CAGTGCTCAC ACAGATTGTC TGATGAAAAG TAAATAGCAA GGGGTCTG
GAAGCAGACT GATACTGCTCC CTTCGTCAG AGGCCAGGA CACCGCCCTT TCACGGGGT AACAGGGTT
CGAATCCCT AGGGGACGCC ACTTGCGGG TAATGTTGTA AAGCGTTGCC ATCACTATCT CAAAACTGAC
TTACGAGTCA CGTTTGAGAT ATTGCTCTT TAAAAATCTG GATCAAGCTG AAAATTGAAA CACAGAACAA
CGAAAAGTTGT TCGTGAGTCT CTCAAATTG TAATGAAATCG TGATGAAACGA CGCAACACCGA TGA
TGA

(SEQ ID NO 135)

Figure 61

CCTTAAAGAA CTGTTCTTGT AAGTGCTCAC ACAGATTGTC TGATGAAAAA CGAGCAGTAA AACCTCTACA
GGCTTGTAGC TCAGGGTGGTT AGAGGCACCC CCTGATAAGG GTGAGGTCGG TGTTCAAGT CCACTCAGGC
CTACCAAATT TTCCCTGAAT ACTGCGGTGT GAAATAACTC ACATACTGAT GTATGCTTCG TTATCCACG
CCTTGTCTCA GGAAAATTAA TCGGTAAGA GGTTCGTGACT ACACGATGGG GCTATAGCTC AGCTGGGAGA
GGCCTGCTT TGCACGCCAGG AGGTCTGGGG TTTCGATCCCG CATAAGCTCCA CCATCTCGTG AGTGTTCAG
AAAAAAATACT TCAGAGGTGA CCTGAAAGGG TTCACTGCGA AGTTTTGCTC TTAAAAAATC TGGATCAAGC
TGAAAATTGA AACACAGAAC AACGAAAGTT GTTCGTGAGT CTCTCAAATT TTCGCAACAC G

(SEQ ID NO 136)

Figure 62

CCTTAAGAA GCGTACTTG AAGTGCTCAC ACAGATTGTC TGATGAAAAG TGAATAAGCAA GGC GTCTTGC
GATTGAGACT TCAGTGTCCC CTTCGTCTAG AGGCCAGGA CACCGCCCTT TCACGGGGGT AACAGGGGGT
CGAATCCCC AGGGGACGCC AGCGTTCAAA CTGATGAGGT CAAACCTCCA GGGACGCCAC TTGCTGGTT
GTGAGTGAAA GTCACCTGCC TTAATATCTC AAAACTGACT TAGGAGTCAC GTTTGAGATA TTGCTCTT
AAAATCTGG ATCAAGCTGA AAATTGAAAC ACAGAACAAAC GAAAGTTGTT CGTGAGTC CCAAATTTC
GCAAACACGAT GATGAAATCGT AAGAAACATC TTGGGGTTGT GA

(SEQ ID NO 137)

Figure 63

CCTTAAGAA ACCGGTCTTG AAGTGCTCAC ACAGATTGTC TGATGAAAAA CGAGCAGTAA AACCTCTACA
GGCTTGTAGC TCAGGTGGTT AGAGGGCACC CCTGATAAGG GTGAGGTGG TGAGGTCAAGT CCACTCAGGC
CTACCAAATT TTCCCTGAAT ACTGCGTTGT GAAATAACTC ACATACTGAT GTATGCTTCG TTATTCCACG
CCTTGTCTCA GGAAAATTAA TCGGTAAAGA GGTTCTGACT ACACGATGGG GCTATAGCTC AGCTGGGAGA
GGCCCTGCTT TGCAAGCAGG AGGTCTGCCG TTCGATCCCG CATAGCTCCA CCATCTCGTG AGTGTGTTACG
AAAATACT TCAGAGTGTAA CCGAAAGGG TTCACTGGGA AGTTTTGCTC TTAAAATC TGGATCAAAGC
TGAAAATTGA AACACAGAAC AACGAAAGTT GTTCGTGAGT CTCTCAAATT TTGGCAACAC GATGATGAAT
CGTAAGAAC ATCTTCGGGT TTGTA

(SEQ ID NO 138)

Figure 64

CTAAGGATAT ATTGGAAACA TCTTCTTCGG AAGATGGGA ATAACGTGAC ATATTGTATT CAGTTTGAA
TGTTTATTAA ACATTCAAAT ATTTTTGTGTA TAAAGTGATA TTGCTTTGA AAATAAGCA GTATGGAGC
GCTTGACTAA AAAAATTGT ACATTGAAA CTAGATAAGT AAGTAAAATA TAGATTTCAC CAAGCAAAAC
CGAGTGAATA AACAGTTTA AATAAGCTTG AATTCTATAAG AAAATAATCGC TAGTGTTCGA AGAACACACTC
ACAAGATTAA TAACGGGTAA AAATCTTTT ATAAAAGAAC GTAACCTCAT GTAACGTTT GACTTAAAA
AATGGGGAA ACATA

(SEQ ID NO 139)

Figure 65

CTAAGGATAT ATTGGAAACA TCTTCTTCAG AAGATGCCA ATAACGTGAC ATATTGTATT CAGTTTGAA
TGTTTATTAA ACATTCAAAT ATTTTTTGGT TAAAGTGATA TTGCTTATGC GAGCNCITGA CAATCTATT
TTTTAAAGA AAGGGGTGT CAGACAATGC ATTAAGAAAA ATTAAAGCGG AGTTTACTTT TGTAATGAG
CATTGATT TITGAAATA AAGCAGTATG CGAGCGCTTG ACTAAAAAGA AATTGTACAT TGAAAACCTAG
ATAAGTAAGT AAAATATAGA TTTACCAAG CAAAACCGAG TGAATAAAGA GTTTAAATA AGCTTGAAATT
CATTAAGAAAT ATTGGCTAGT GTTCGAAGA ACACTCACAA GATTAATAAC GCGTTAAAT CTTTTATAAA
AAGAAAACGT TTAGCAGACA ATGAGTTAA TATTTAA GCAGAGTTA CTTATGTAAA TGAGCATTAA
AAATAATGAA AACGAAGCCG TATGTGAGCA TTGACTT AAAATGGTG GAAACATA

(SEQ ID NO 140)

Figure 66

CTAAGGATAT ATTCGGAACA TCTTCTTCAG AAGATGCCGA ATAACGTGAC ATATTGTATT CAGTTTGAA
TGTTTATTAA ACATTCAAAT ATTTCGGTGT TAAAGTGATA TTGCTTATGC GAGCGCTTGA CAATCTATTG
TTTTTAAGA AACGGGTTGT CAGACAATGC ATTAAGAAA ATAAAGCCG AGTTTACTTT TGTAATGAG
CATTGATT TTGAAATA AAGCAGTATG CGAGGGCTG ACTAAAANGA AATTGTACAT TGAAAACTAG
ATAAGTAAGT AAAATATAGA TTTTACCAAG CAAAACCGAG TGAAATAAAGA GTTTGAAATA AGCTTGAAATT
CATAAAGAAT AATCGCTAGT GTTCGAAAGA ACACTCACAA GATTAATAAAC GGTTTAAAT CTTTTATAAA
AAGAACGTAACCTCATGTAA ACCGTTTGACT TATAAAATG GTGGAAACAT A

(SEQ ID NO 14.1)

Figure 67

CTAAGGATAT ATTCGGAACA TCTTCTTCAG AAGATGCCGA ATAACGTGAC ATATTGTATT CAGNTTGAA
TGTTTATTAA ACATTCAAAA AATGGGGCTTA TAGCTCAGCT GGTTAGAGCG CACGCCTGAT AAGCGTGAGG
TCGGTGGTTC GAGTCCACTT AGGCCCAACCA TTATTGTAC ATTGAAAAGTAA AGATAAGTAA GTAAAATATA
GATTTACCA AGCAAAACCG AGTGAATAAA GAGTTTAAA TAAGCTTGAA TTCATAAGAA ATAATCGCTA
GTGTTCGAAA GAACACTCAC AAGATTAAATA ACGGCGTTAA ATCTTTTAT AAAAGAACGT AACTTCATGT
TAACGTTGA CTATAAAAAA TGGTGGAAAC ATA

(SEQ ID NO 142)

Figure 68

CTAAGGATAT ATTGGAAACA TCCTTCYTCAG AAGATGCCGA ATAATGTGAC ATATTGTATT CAGTTTGAA
TGTGTTATTAA ACATTCAAAT ATTGTTGGT TAAAGTGATA TTGCTTATGC GAGCGCTTGA CTAAGGAA
ATTGTACATT GAAACTAGA TAAGTAAGTA AAANTATAGA TTGCTTACCAAG CAAACCCGAG TGAAATAAAGA
GTTTAAATA AGCTTGAATT CATAAGAAAT AATCGCTAGT GTTCGAAAGA ACACTCACAA GATTAATAAAC
GCGTTAAAT CTTTTATAA AGAACGTAA CTCATGTTA ACGTTTGACT TATAAAATG GTGGAAACAT

A

(SEQ ID NO 143)

Figure 69

CTAAGGATAT ATTGGAAACA TCTTCTACGA AGATGAGGGA ATAACGTGAC ATATTGTATT CAGTTTGAA
TGTTTATAA CATTCATTTG TACATTGAAA ACTAGATAAG TAAGTAAGAT TTTACCAAGC AAAACCGAGT
GAATAGAGTT TAAATAAGC TTGAATTCAAT AAATAATCGC TAGTGTTCGA AAGACNTCCA CAAGATTAAAT
AACTAGTTT AGCTATTAT TTTGAATAAC AATTCAAAT ATTCAAAAT ATGGTGGGAC ATA

(SEQ ID NO 144)

Figure 70

AAGGATAAGG AACTGCACAT TGGTCTTGTT TAGTCTTGAG AGGTCTTG TG GGGCCTTAGC TCAGGCTGGGA
GAGGCCCTGC TTTCACCGCA GGAGGTCAAGC GGTTCGATCC CGCTAGGCTC CATTGGTCAAG AGATCACCAA
GTAATGCACA TTGAAAATTG AATATCTATA TCAAATAGTA ACAAGAAAAT AAAACCGAAAAA CGCTGTAGTA
TTAATAAGA GTTTATGACT GAAAGGTCAA AAAATAA

(SEQ ID NO 145)

Figure 71

AAGGAAATGG AACACGTTTA TCGTCTTATT TAGTTTGAG AGGTCTTGTG GGGCCTTAGC TCAGCTGGGA
GAGGCCCTGC TTNGCACGCA GGAGGTAGC GTTCGATCC CGCTAGGCTC CATCAGGATA CANTCCCTACT
AAACTTATA CAAGTGAAGT TGAACACGCA ACTCACTCC TAGGAAATA GACAATCTTC GCTTGTGTGC
AAGGCACACA TGGTCAGATT CCTAATTTC TACAGAAAGT TCGCTAAGC GAGCGTTGCT TAGTATCCTA
TATAATAGTC CATNGAAAAT TGAATATCTA TATCAAATTC CACGATCTAG AAATAGATTG TGGAAACGTA
ACAAGAAATT ACCCGNAAA CGCTG

(SEQ ID NO 146)

Figure 72

AAGGATAAGG AACTGCCACAT TGGTCTTGT TAGTCTTGAG AGGTCTTGTG GGGCCTTAGC TCAGCTGGGA
GAGCGGCCTGC TTGCAACGCA GGAGGTCAAGC GGTTTCGATCC CGCTAGGCTC CATTGGTGTG AGATCACCAA
GTAATGCCACA TTGAAAATTG AATATCTATA TCAAATAGTA ACAAGAAAT AACCGAAC GCTGTAGTAT
TAAAAGAGTT TATGACTGAA AGGTCAAGAA ATAA

(SEQ ID NO 147)

Figure 73

CTAAGGATAT ATTGGAAACA TCTTCTTACG AAGATGCAGG ATAACATTG ACATATTGTA TTCAGNTGTG
AATGCTCATT GGAGNATTCA TNGCATNATT TGGTNCATTG ACANCTAGAT AGNAAGTAA ATTATATGAT
TTTACCAAGC AAAACCGAGT GAATTAGAGT TNTNNAACAA GCTTTGATT CAAAAGAAA TAATCGCTAG
TGTTCGAAAG AACACTCACA GATTANTAAC ATCTTGGGT TTCACCCGAC TTGTTCGNT CGAAAGTCAA
AAAA

(SEQ ID NO 148)

Figure 74

AAGGATAAGG AACTGGCAT TGGTCTTGT TAGTCTTGAG AGGTCTTGTG GGGCCTTAGC TCAGCTGGGA
GAGGCCCTGC TTTCACGC GGAGGTCAAGC GTTTCGATCC CGCTAGGCTC CATTGGTGAG AGATCACCAA
GTAATGCACA TTGAAATATG AATATCTATA TCAAATAGTA ACAAGAAAAT AAACCGAAAA CGCTGTAGTA
TTAATAAGAG TTATGACTG AAGGTCAAA AAATAA

(SEQ ID NO 149)

Figure 75

AAGGATAAAGG AACTGGCGCAT TGGTCTTGTT TAGTCTTGAG AGGTCTTGAG GGGCCTTAGC TCAGGCTGGGA
GAGCGGCCTGC TTGCAACCCA GGAGGTCAAGC GGTTCGATCC CGCTAGGCTC CATTGGTGAG AGATCACCAA
GTAATGCACA TTGAAAATTG AATATCTATA TCAAATAGTA ACAAGAAAT AAACCGAAAA CGCTGTAGTA
TTAATAAGAG TTATGACTG AAAGGTCAAGA AAAATAA

(SEQ ID NO 150)

Figure 76

AAGGAAAAGG AACTGGGCAT TGGTCTTGGTT TAGTCTTGAG AGGTCTTGTG GGGCCTTAGC TCAGCTGGGA
GAGCGCCTGC TTTGCCACGCA GGAGGTCAAGC GGTTCGATCC CGCTAGGCTC CATTGGTGAG AGATCACCAA
GTAATGCACA TTGAAAATTG AATATCTATA TCAAATAGTA ACAAGAAAAT AAACCGAAAA CGCTGTAGTA
TTAATAAGAG TTTATGACTG AAGGGTCAGA AAAATAAA

(SEQ ID NO 151)

Figure 77

AAGGATAAGG AACTGGCCAT TGGTCTTGTT TAGTCTTGAG AGGTCTTGTC GGGCCTTAGC TCAGCTGGGA
GAGGCCCTGC TTGCA CGCA GGAGGTCAAGC GTTTCGATCC CGCTAGGCTC CATTGGTGGAG AGATCACCAA
GTAATGCACA TTGAAATATG AATATCTATA TCAAATAGTA ACAAGAAAAT AACCGAAC GCTGTAGTAT
TAAAAGAGTT TATGACTGAA AGGTCAAGAA ATAA

(SEQ ID NO 152)

Figure 78

AAGGATAAGG AACTGGCAT TGGTCTTGT TAGTCTTGAG AGGTCTTGTG GGGCCTTAGC TCAGCTGGGA
GAGGCCCTGC TTTGCACGCA GGAGGTCAAGC GGTTCGATCC CGCTAGGGCTC CATTGGTGAG AGATCACCAA
GTAATGCACA TTGAAAATTG AATATCTATA TCAAATAGTA ACAAGAAAT AACCGAAC GCTGTAGTAT
TAAAAGAGTT TATGACTGAA AGGTCAAAA TAA

(SEQ ID NO 153)

Figure 79

TAAGGAAGAT CGAGAATTGG AAAGAGGTCG GATTATCCG GATGATCCTT CTCCATCTTA TTAGAACATA
GATCGCAGGC CAGTCAGCCT GACCGATCGCT TGCAGGGGTG CCGCCTTCGT TTCTCTTTCT TCATTGTTGA
TTGCTCACGG GCGTACCGC AGCTGACCGT GCTGGCCCTG CGCAGGGCGC GCCCATCAGG GCCGAACGGC
CGGCTGGCCT TGCNAAGCCT CGCTTCGGGG TGGATCTGTG GATCGGGTAG TAGCGGTATCT
GGGCTTGTAG CTCAGTTGGT TAGAGCACAC GCTTGATAAG CGTGGGGTGC GAGGTTCAAG TTCTCCCAGG
CCCACCAAGT TACTTGTAGA GGGGCCGTAG CTCAGGTGGG AGAGCACCTG CTTTGCAGC AGGGGGTCGT
CGGTTCGATC CCGTCCGGCT CCACCATCAT GTTGGTGGTG AGACGGATAT TGCCAATCAA CAAAGAAAG
AAACAAGTT GCGGACTNTT ACGAAAGT GCCTGTTCTG TATGAAATCG TGAAGAAAG ATGTAATCGG
ATCAACTGAA GAGTTGATGT CGCAAGAACCT TGCTCAAGC CTGCTAAAT GATTGATGTG TTTAACCGCC
ATCACCGATT GTATCTCGAG AAGCTGGTCT TTCTGCTGAT ACTGTTGAAA CGAGCATTTG CAGTCGNATG
GCAACATTG GCGTCGCATA ATGGGGCTT AAGAGGCTGAG TTTGATGGA TATTGGCAAT GAGAGTGTAC
AAGTGTCTTA AGGGCATTGG TGGATGCCCT GGCAATGCAC

(SEQ ID NO 154)

Figure 80

AAGGAGGCC ACCGAGAAACA CTCCAAATTGG TGGGGTGTAA GCCGGTGAGGG GTtCTCGTCT GTAGTGGACG
GAAGGCCGGGT GCACAAACAAC AAGCAAGCCA GACACACTAT TGGGTCCCTGA GGCAACATCT CTGTTGGTT
CGGGATGTTG TCCCACCATC TTGGTGGTGG GGTGTGGTGT TTGAGAATTG GATAAGTGGTT GCGAGGCATCA
ATGGATGCG CTGCCTTTG GTGGCGTGT ATTATATTCT TTGGTTTTG TGTTAT

(SEQ ID NO 157)

Figure 81

AAGGAGGCACC ACGGAGAAACA CCCCAATTGG TGGGGGTGTGA GCCGGTGAGGG GTTCTCGTCT GTAGTGGACG
AGGGCCGGGT GCACAAACAAAC AGGCAATCGC CGGACACACT ATTGGGCCCT GAGACAAACAC TCGGCCGACT
GAGGTGAGC TGTTGTCCT CCATCTTGGT GGTGGGGGT GGTTGTTGAG CATTGAATAAG TGTTTGGAG
CATCTAGCCG GATGGCTTCC CCAGTGGTGC CGTTCGTCA AAAATGTGTA ATTTTTCTT TTGTTTGT
GTTCGT

(SEQ ID NO 158)

Figure 82

AAGGAGGCACC ACGAGAAACA CCCCAATTGG TGGGGTGTGA GCCGGTGAGGG GTTCTCGTCT GTAGTGGACG
AGGGCCGGGT GCACAAACAAAC AGGCAAATCGC CGGACACACT ATTGGGCCCT GAGACAACAC TCGGCCGACT
GAGGGTCGACG TGGTGTCCCT CCATCTTGGT GGTGGGGTGT GGTGGTTGAG CATTGAATAAG TGTTGGCAG
CATCTAGACG GATGGGTTCC CCAGTGGTGC GCGTTCGTCA AAAATGTGTA ATTTTCTTT TGTTTTGT
GTTCGT

(SEQ ID NO 159)

Figure 83

AAGGAGCACC ACGAGAAACA CCCCAATTGG TGGGGTGTGA GCCCGTGAGGG GTTCTCGTCT GTAGTGGACG
AGGNNCGGGT NNACAACAAC NGCCAATCGC CGGACACACT ATTGGGNCCCT GAGACACAC TCGGCCGACT
GAGGTGACG TGTTGTCCTT CCATCTTGGT GGTGGGGTGT GGTTGTTGAG CATTGAATAAG TTGTTGCGAG
CATCTAGCCG GATGCCGTTCC CCAGTGGTGC CGGTTCGTCA AAAATGTGTA ATTTCCTNT TTGTTTTGT
GTTCGT

(SEQ ID NO 160)

Figure 84

AAGGAGGCC ACCGAGAAACA CTCCAATTGG TGGAGTGTGA GCCGTTGAGGG GTTCTCGTCT GTAGTGGACG
AGGGCCGGGT GCACAAACAGC AGACAATGCC CAGACACACT ATTGGGCCCT GAGACAACAC TCGGCCGACT
TTGGTCAACG TGGTGTCCCT CCATCTTGCT GGTGGGGTGT GGTGGTTGAG CATTGAATAAG TGTTGGAG
CATCTAGACG GATGGCGTTGC CCTCGGGCCG CGTGGTCGTC AAAAATGTGT AATTTTTCT TTGGTTTT
GTGGTCACT

(SEQ ID NO 161)

Figure 85

AAGGAGCACC ACGAGAAACCA CTCCAATTGG TGGAGTGTGA GCCGGTGAGGG GTTCTCGTCT GTAGTGGACG
GGAGCCGGGT GCACAACAAAC AGGCAATCGC CAGACACACT ATGGGCCCT GAGACAAACAC TCGGGCCGGCT
TTGAGTCGAA GTGGTGTCCC TCCATCTTGG TGTTGGGTG TGTTGTTGA GCATTGAATA GTGGTTGCGA
GCATCTAGAC GGATGCCGTG CCTTCGGGCC GCGTGTTCGT CAAAAATGTG TAATTTC TTTGGTTT
TGTGTTCGT

(SEQ ID NO 162)

Figure 86

AGGGAGCACC GNAAACGCAT CCCGGCTGGG GTCTGGGTTC GGCCTGTTGT CGCGTGGNC CGAGGTGTTG
GGCAGCAGGC AGTAACCNCC GGAACACTGT TGGTTTTGA GNNAACACCC GTGGTGGGT TTGCTCCCC
GTGGTGNCGG GGTGTGGGTG TTGAGTGTG GATAAGTGGTT GCCAGCATCT GCCAAAGACT GTGGTAAGCG
GTTTTGTG ANTGTTCCT GGTGTTGT

(SEQ ID NO 163)

Figure 87

AAGGAGCACC ACCGAGAAACA CTCCAATTGG TGGGGTGTGA GCCGTGAGGG GTTCTCGTCT GTAGTGGACG
AGGGNCGGGT GCACAAACAAAC AGNCAATCGC CAGACACACT ATTGGNCCT GAGACAAACAC TCGGCCGACT
TNGGTTGAAG TGGTGTCCCT CCATCTTGGT GGTGGGGTGT GGTTGTTGAG TATTGGATAG TGCTTGGAG
CATCTAANTG AACGGCGTGC CGNCAACGGT TACGTGTCAA TTTCGTCTAT TTNTTTCTAT TGGTTTTGT
GTTCGT

(SEQ ID NO 164)

Figure 88

AAGGAGCACC ACGAGAACCA CTCCAATTGG TGGGGTGTGA GCCGTGACGG GTCTCGTCT GTAGTGGACG
AGGGCCGGGT GCACAAACAC AGGCAATCGC CAGACACACT ATGGNCCCT GAGACAACAC TCGGCCGACT
TTGGTCAAG TTGGTGTCCC CCATCTTGGT GGTTGGGTGT GGTTGGTAG TATTGGATAG TGTTGGCGAA
CATCTAAATG AACGGCTTGC CGGCAACGGT TACGGTGTTCG TTTTAGTGTAA ATTNTTTCTA ATGGTTTGT
TGTTCGT

(SEQ ID NO 165)

Figure 89

AAGGAGGCC ACCAGAACCTG GGCGGGCCCC GCAGATCGCG GGATCAGCTG AGCTTCAGG CGATTCTGTG
GATGGCCTCG CACCTGTAGT GGGTGGGGT CTGGTGCACT CAACAAACTT GGC GTGGGAT GCGGGAAAGC
ATCTGCGGA AATCATCAGA CACACTATG GGCTTTGAGA CAACAGGCC GCAGNCCTGN CCCGTTGGGG
GCAGNGGTG TGTGTTGCC TCACTTTGGT GGTGGGGTG GTGTTGATT TGTGGATAGT GTTGCAGC
ATCTAGGGCG CAGAATGTGT GGTCTCACTC CTTGTTGGTG GGGCCTGGTT TTGATGCCA TTGATGGCA
ATTCTTTG AACTCATT TTGTTTTT GTGTTGT

(SEQ ID NO 166)

Figure 90

AAGGAGCACC ACCAAAAACT CCCCAATTGG TGGGGTGTAA GCGCTGAGGG GTTCCCGTCT GTAGTGGACG
GGGGCCGGGT GCGCAACAGC AAGCGAAACG CCGGACACAC TATTGGGTCC TGAGGCAACA CTCGGGTTTG
TCCCCCTCAG GGATTTCTG GGTGTTGTC CACCATCTTG GTGGTGGGT GTGGTGTGG AGAATTGGAT
AGTGGTTGCG AGCATCAAAT GGATGGCGTGTG CCCCTACGGG TAGCGTGTTC TTGCGCAA TTTTATTGNT
TGGTTTTGT GTTGT

(SEQ ID NO 167)

Figure 91

AAGGAGCACC ACGAGAAGCA CTCACACTGG TGGGGTGCAC GCGGTGAGGG GTTCTCGTCT GTAGTGACG
AGAGCCGGGT GCGGACAAC GAAAGGCCA GACAGGCCA GACACACTAT TGGGTCCCTGA GGCAACACTC GGGCTTGCC
AGAGCTGTG TCACCCACATC TTGGTGGTGG GGTGTGGTGT TTGAGAATTG GATAAGTGGTT GCGAGCATCA
AATGGATGGC TTGCCCTAC GGTTGGCGTG TTCTGGTTG CAATTTATT CTTGGTTT TGTGTTTGT

(SEQ ID NO 168)

Figure 92

AAGGAGCACC ACGAAAAACA CCCCAAACGG TGCGGTGTTAA GCCGTGAGGG GCTCCCGTCT GTAGTAGACG
GGCGCCGGGT GCGCAACAGC AAGCGAGCCA GACACACTAT TGGGTCTGA GGCACAACTC GGGCTTGCT
TGGACTCGTC CAAGAGTGT GTCCCCACCAT CTTGGTGGTG GGGTGTGGT TTGAGAATT GGATAAGTGGT
TGCAGGCCATC ANCTGGATGC GTTGGATGC GGGGTAGCGT GTCTTTGT GCAATTNTAT TCNNTGGTT
TTGTGTTAGT

(SEQ ID NO 169)

Figure 93

AAGGAGCACC ACCAAAAACA CTCGGCATCC GGTGGGGTGT GAGCCGTGAG GGAGCCCCGTG CCTGTACTGG
GTGTGGGTG GGTGGCGGAC AACAAATGGG AAAAATCGCT GGGCACACTA TTGGGGCTTTG AGGCCAACACC
TGGTTTGTG TGGTGGTGT CGCTCCATCT TGTTGGTGGG GTGTGGTGTG TTGAGTTGTGG ATAGTGGTGTG
CGAGGCATCTA AGCAAAAGCT GTTGTGTTGAC GGTTTTTGTC GAGTGTGTG TGTGT

(SEQ ID NO 170)

Figure 94

AAGGAGGCC ACCAAAAACA CTCCAATTGG TGGGGTGTAA GCCGTTGAGGG GTCTCATCT GTAGTGGACG
AGAGCCGGGT GCACAAACAGC AAATGAATCG CCAGACACAC TGTGGGTCC TGAGGCAACA CTCAGGCTTG
TCCCATGTTG GGCTTGATCG GGTGCTGTCC CCCATCTG GTGGTGGGT GTGGTGTGG AGTATTGGAT
AGTGGTTGCC AGCATCTAAA TGGATAACGTT GCCAGTAATG GTGGCGTATT CATTGAAAT GTGTAATT
CTTCTTTGGT TTGTGTGT

(SEQ ID NO 171)

Figure 95

AAGGAGCACC ACGAAAACA CTCCAATTGG TGGGGTGTAA GCCGTGAGGG GTTCTCATCT GTAGTGACG
AGAGCCGGGT GCACAAACAGC AAATGAATCG CCAGACACAC TGTTGGGTCC TGAGGCAACA CTCAGGCTTG
TCCCATGTTG GGCTTGATCG GGTGCTGTCC CCCCATCTTG GTGGTGGGGT GTGGTGTGTT AGTATTGGAT
AGTGGTTGCG AGCATCTAAA TGGATAACGTT GCAGTAATG GTGGCGTGT CATTGAAAAT GTGTAATTGTT
CTTCTTGGT TTGTTGTT

(SEQ ID NO 172)

Figure 96

AAGGAGCCACC ACGAAAAACA CTCCAATTGG TGGGGTGTAA GCCCGTGAGGG GTTCTCATCT GTAGTGGACG
AGAGCCGGGT GCACAAACAGC AAATGAATCG CCAGACACAC TGTGGGTTC TGAGGCAACA CTCAGGGCTTG
TCCCATGTTG GGCATTGATCG GGTGCTGTCC CCCCATCTTG GTGGTGGGT GTGGTGTG AGTATTGGAT
AGTGGTTGCC AGCATCTAAA TGGANACGTT GCCAGTAATG GTGGCGGTGT CATTGAAAT GTGTAATT
CTTCTTTGGT TTGTTGTT

(SEQ ID NO 173)

Figure 97

AAGGAGCACC ATTCTCAGT CGAATGAAC T GAGAACATAA AGCGAGTATC TGTAGTGGAT ACATGCTGG
TGAATATGTT TTATAATCC TGTCCACCC GTGGATAGGT AGTCGGCAA ACGTCGGACT GTCATAAGAA
TTGAAACGCT GGCACACTGT TGGGTCTGA GGCACACAT TGTGTTGTCA CCCTGCTTGG TGCTGGGGTG
TGGTCCTTGA CTTATGGATA GTGGTTGCCA GCATCTAAC ATAGCCTCGC TCGTTTCTGA GTGAGGCTGG
TTTGTGCAAT TTTATTAGCT

(SEQ ID NO 174)

Figure 98

CCTAATGATA TTGATTCCCG TGAAGTGCCTC ACACAGATTG TCTGATGAAA AAGTAACCGAG CAGAAATACCC
TTTATAGGCT TGTAGCTCAG GTGGTTAGAG CGCACCCCTG ATAAGGGTGA GGTGGGTGGT TCAAGTCCAC
TCAGGCCTAC CACTTCTCGA AGTGGAAAAG GTACTGCACG TGACTGTATG GGGCTATAGC TCAGCTGGGA
GAGCGCCTGC CTTGCACGCC GGAGGTCAGC GGTTCGATCC CGCTTAGCTC CACCATAG TCCTGTATT
CAATACTTCA GAGTGTACTG GCAACAGTAT GCTGCGAAGT ATTGTGCTCT TTAACAATCT GGAACAAGCT
GAAAATTGAA ACATGACAGC TGAAACTTAT CCCTCCGTAG AAGTATTGGG GTAAGGATTAA ACCTGTCTATA
GAGTCTCTCA AATGTAGCAG CACGAAAGTG GAAACACCTT CGGGTTGTGA

(SEQ ID NO 195)

Figure 9

CCTAATGATA TTGATTCCGG TGAAGTGCCTC ACACAGATIG TTTGATAGAA ACGTAATGAG CAAAAGGGCT
ACCTGTTGAT GTAATGAGTC ACTGACTCAT GCTGATAAG ACCGATTAAG ACAGTCAGTT TAATCGGATT
TTCGTGTCCC CATCGTCTAG AGGCCTAGGA CACTGCCCT TCACGGCTGT AACAGGGTT CGAATCCCCT
TGGGACGCC ATTGCGATAAT GAGTGAAGA CATTATCACC GGTTCTTGGAA ACCGAAACAA TCTTAAGAT
GACTCTTGCG AGTCGTGTT AAGATATTGC TCTTTAACAA TCTGGAACAA GCTGAAAATT GAAACATGAC
AGCTGAAACT TATCCCTCG TAGAAGTATT GGGGTAAGGA TAAACCTGTC ATAGAGTC TCAAATGTAG
CAGCACGAAA GTGGAAACAC CTTCGGGGTG TGA

(SEQ ID NO 196)

Figure 100

TAAGGATAAG GAAAGAAGCCT GAGGAAGGTT CTGACTAGGT TGGCCAAGCA TTTATATGTA AGAGCAAGCA
TTCTTATTCA TTTCGTGTTGT TAAGGAGTAGC GCGGTGAGGA CGAGACATAT AGTTTGTGAT CAAGTATGTT
ATTGTAAGA AATAATCATG GTAACAAGTA TATTTCACGC ATAATAATAG ACGTTTAAGA GTATTGTCT
TTTAGGTGAA GTGCTTGAT GGATCTATAG AAATTACA

(SEQ ID NO 197)

Figure 101

TAAGGATAAG GAAACCTGTG AATCTTTTC CCTTCTTTG TTCAGTTTG AGAGGTTCAT CTCTCAAAAC
GTGTTCTTG AAAACTAGAT AAGAAAAGTT AGTGTAAAAA GACGAAGAGA AACCGTAGGT TT'TTCTTCAA
CCAAAACCGA GAATCAAACC GAGAAAGAAT CTTTCCGTT TCATAAGCGA TCCGACGTT ATGAAAACAC
AACAAACACT TCGTAAGAAG GATGA

(SEQ ID NO 213)

Figure 102

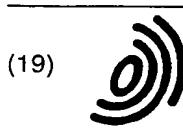
TAAGGATAAG GAAACCTGTG AATCTTTTC CCTTCTTTTG TTCAGTTTG AGAGGGTCAAT GACGGCTCAT
CTGAGTACCA GGTGACACGTT TTTGAGGGT TCTCTTCGTA TGAGGGCCCT ATAGCTCAGC TGGTTAGAGC
GCACGCCCTGA TAAGCGTGA GTCGGTGGTT CGAGTCCACT TAGGCCCACT TTTTTGAATA AACCTTCTT
TTTATATGT TAATAAGGGG CCTTAGCTCA GCTGGAGAG CGCCTGCTTT GCACGCCAGGA GGTCAAGCGGT
TCGATCCGC TAGGCTCCAC CAAAGATACT TTGTTCTTTG AAAACTAGAT AAGAAAAGTT AGTGTAAAAA
GACGAAGAGA AACCGTAGGT TTTCTTCAA CCAAAACCGA GAATCAAACC GAGAAAGAAT CTTTCCGTTT
TCATAAGCGA TCGCACGTT ATGAAAACAC AACAAACAC' TCGTAAGAAG GATGA

(SEQ ID NO 214.)

Figure 103

TAGGATAAG GAAACCTGTG AATCTTTTC CCTTCTTTTG TTCACTTTTG AGAGGTCAAT GACGCTCAT
CTGAGTACCA GGTGACACT TTTTGAGGTG TCTCTTCGTA TGAGGGCCT ATAGCTCAGC TGTTAGAGC
GCACGCCCTGA TAAGCGTGA GTCGGTGGTT CGAGTCCACT TAGGCCACT AACCTTTCTT
TTTTATATGT TAATAAGGG CCTTAGCTCA GCTGGGAGAG CGCCTGCTTT GCACGCCAGGA GGTCAAGGGT
TCGATCCCCC TAGGCTCCAC CAAAGATAGT TTGTTCTTGT AAAACTAGAT AGAAAAGTT AGTGTAAAAA
GACGAAGAGA AACCGTAGGT TTTCTTCAA CCAAAACCGA GAAAGAACATT TTCCGTTTC ATAAGCGATC
GCACGTTAT GAAAACACAA CAACACCTC GTAAGAACGA TGA

(SEQ ID NO 215)



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(54) Simultaneous detection, identification and differentiation of Eubacterial taxa using a hybridization assay

(57) The present invention relates to a method for detection and identification of at least one micro-organism, or for the simultaneous detection of several micro-organisms in a sample, comprising the steps of:

- (i) if need be releasing, isolating or concentrating the polynucleic acids present in the sample;
- (ii) if need be amplifying the 16S-23S rRNA spacer region, or a part of it, with at least one suitable primer pair;
- (iii) hybridizing the polynucleic acids of step (i) or (ii) with at least one and preferably more than one of the spacer probes as mentioned in table 1a or equivalents of thereof, under the appropriate hy-

bridization and wash conditions, and/or with a taxon-specific probe derived from any of the spacer sequences as represented in figs. 1-103 under the same hybridization and wash conditions;
(iv) detecting the hybrids formed in step (iii) with each of the probes used under appropriate hybridization and wash conditions;
(v) identification of the micro-organism(s) present in the sample from the differential hybridization signals obtained in step (iv).



European Patent
Office

EUROPEAN SEARCH REPORT

Application Number
EP 01 20 0042

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The present search report has been drawn up for all claims			
Place of search	Date of completion of the search	Examiner	
BERLIN	14 February 2001	De Kok, A	
CATEGORY OF CITED DOCUMENTS		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons S : member of the same patent family, corresponding document	
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document			



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Application Number

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Place of search	Date of completion of the search	Examiner			
BERLIN	14 February 2001	De Kok, A			
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T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document					

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